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OCULAR EFFECTS OF ALTITUDE FLYING AND OF DEEP SEA DIVING

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The subject assigned refers primarily to changes brought about by alterations in atmospheric pressure and in partial pressure of oxygen, to rapid and severe changes in temperature and to protection of the eyes against glare, air blast, dust and flying debris. Changes in atmospheric pressure in flying are within the range between the pressure at sea level (1 atmosphere—about 15 pounds per square inch [1,050 Gm. per square centimeter], or 760 mm. of mercury) and a pressure of about ⅙ atmosphere (2½ pounds per square inch [170 Gm. per square centimeter], or 127 mm. of mercury) at the maximum altitudes now attainable by military aircraft. Pressures encountered in deep sea diving can also be expressed in terms of pressure at sea level. These pressures range from 1 to 6, 7 or 8 atmospheres.

The physiologic effects of variations in pressure are brought about in several ways:

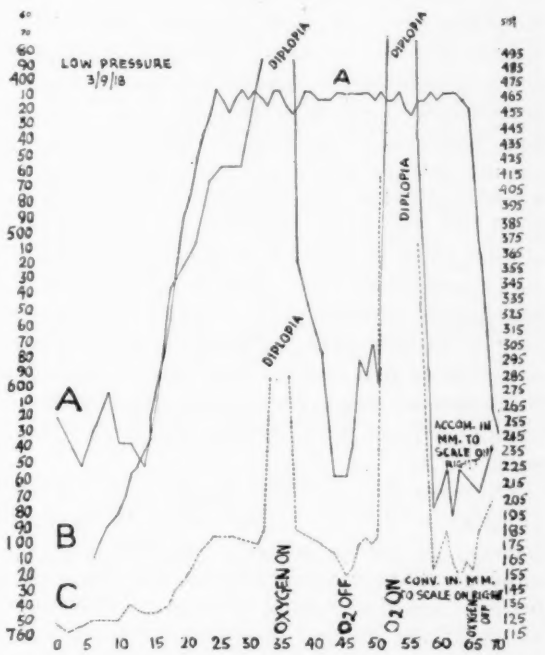
1. By increase or decrease in the partial pressure of the oxygen.

2. By rapid decompression of the envelope of air around the earth, resulting in escape of inert gases from solution in bodily fluids and tissues in the form of bubbles, or air emboli, which tend to obstruct capillaries and small blood vessels and to produce disturbances of function through localized ischemia or through direct pressure on the brain and nerve tissues.

3. Through the toxic effects of oxygen. These effects have been reported occasionally at greatly increased pressures, such as those experienced by divers, and also when oxygen was added to inspired air.

As can be seen from the foregoing remarks, ocular effects may occur either as part of a general anoxic syndrome or as accidents resulting from localized obstruction or from phenomena due to direct pressure which affect the nutrition of the retina or the innervation of the intrinsic or extrinsic ocular muscles.

Inasmuch as military flying at altitudes above 10,000 feet (3,300 meters) requires the use of oxygen, severe degrees of anoxia are not often encountered. However, failure of the supply of oxygen or leakage of masks at great altitudes may cause rapidly developing and severe anoxia, with a resultant general picture of failure of special senses, impairment of judgment, loss of consciousness, motor convulsions and anoxic death if the situation is not speedily corrected.



The effect on accommodation and convergence of simulated altitude in the low pressure chamber. *A*, curve of accommodation plotted against figures in millimeters on the right. *B*, curve of barometric pressure plotted against barometric pressure in millimeters on the left. *C*, curve of convergence plotted against a millimeter scale on the right. Note that accommodation and convergence fail when the barometric pressure drops to 400 mm. of mercury. Accommodation and convergence are immediately restored to normal by the administration of oxygen, even though the barometric pressure remains at 400 mm.

Certain effects of even slight or low grade anoxia are reflected in vision to some degree. Prolonged flight at an altitude of 8,000 to 10,000 feet (2,600 to 3,300 meters) causes slight but measureable impairment of retinal response, such as can be demonstrated by diminished perception of low contrast images, increased threshold of

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light sensitivity as demonstrated by the adaptometer test and impaired flicker-fusion response. Slight anoxia has such a definite effect on the sensitivity of the retinal rods that military fliers are advised to cut in their supply of oxygen from the ground on up in combat flying at night. In runs in the low pressure chamber to simulated high altitudes without added oxygen, reduction in visual acuity has been observed in 28 to 65 per cent of persons; color vision has also been impaired. Diminution of sensitivity to red is less than to green or to blue. Under some conditions of anoxia, green and blue signals may appear gray and completely colorless. With regard to the effect of high altitudes on the visual field, reports are somewhat conflicting. Narrowing of the fields, especially of the upper and nasal portions, has been described, but this effect has been attributed by some workers to failure of attention.

Even mild anoxia has been shown to cause a considerable increase in the total area of the normal blindspot, especially under conditions of greatly reduced illumination of the object of the visual test or when low contrast test objects are used. A fasting level of blood sugar exerts a similar effect or may be additive to mild anoxia. In ascents in the low pressure chamber to the equivalent of 19,000 feet (6,000 meters), the area of the blindspot has been found to increase as much as two and one-half times. Reduction to the normal area occurs on the subject's breathing oxygen or on his descent to sea level pressure.

Decrease in intraocular tension at simulated altitudes of 12,000 to 19,000 feet (4,000 to 6,000 meters) in human subjects has been reported, although if low pressure is prolonged the tension tends to return to normal. Pinson [1] in 1940 found no significant changes in intraocular tension in a rabbit decompressed to the equivalent of 40,000 feet (12,000 meters).

In deep sea diving higher pressures are involved, so that anoxia does not play a part. However, disturbances of vision or of muscle balance can be occasioned by a rather infrequent phenomenon known as oxygen intoxication.

Similar systemic effects believed to be caused by nitrogen narcosis have been described in the literature on this subject.

Diplopias, scotomas and amaurosis occur occasionally as a result of sudden reduction of pressure and release of inert gases from saturation. Air emboli probably lodge in the bulbar nuclei, within the optic tract or in the visual cortex, although attempts to demonstrate such phenomena are extremely difficult and have all failed. Investigators have occasionally reported seeing emboli passing through the retinal vessels and through the meningeal vessels which are visible when the calvaria of an experimental animal is removed. Oculomotor disturbances caused by aeroembolism are infrequent; paresthesias, pruritus and other conditions may persist for six to eight hours after exposure to changing pressures but often are of brief duration. The mechanism is not clearly understood.

An indication of the range of ocular disturbances which may be encountered in high altitude flying is given in the following list of complaints referable to the eyes in persons given runs in the low pressure chamber for the purpose of indoctrination. The symptoms are reported as persisting from one to sixty hours: (1) partial blindness, (2) right homonymous hemianopsia, (3) bilateral binasal blurring, (4) nystagmus, (5) spots before the eyes, (6) scintillating scotomas, (7) diplopia, (8) yellow vision and (9) ocular pain.

In addition to phenomena ascribable to lowered partial pressure of oxygen at higher altitudes and to sudden and radical changes in atmospheric pressure, one other problem of some importance has attracted the interest of ophthalmologists. This is the dazzling effect of excessive solar light at upper atmospheric levels. Occasional complaints of excessive brightness at great altitudes are heard. Careful inspection usually fails to demonstrate any unusual local reaction, such as injection of the pupil or ciliary spasm.

For a number of years the medical profession has shown considerable interest in the possible injurious effects of solar rays lying beyond the range of the visible spectrum. The most important in the present connection are the heat waves, the infra-red rays, the visual rays and the ultraviolet rays. Of the waves emitted by the sun, part are completely destroyed in the atmosphere, part are absorbed and part reach the earth. The intensity of all these waves increases with altitude, as the density of the absorbing atmospheric layer decreases. In higher mountains and in flight, therefore, the exposure to ultraviolet, to visible and to infra-red rays is greater than at lower altitudes. Severe sunburn frequently occurs because of exposure to ultraviolet rays, but it has been generally observed that the tolerance of the unprotected eye is apparently considerably greater than that of the skin and of the mucocutaneous junctions. The once hypothesized probability of danger to the eyes from excessive exposure either to infra-red or to ultraviolet rays at high altitude is not now regarded with as great concern as formerly.

1. Pinson, E. A.: Intra-Ocular Pressure at High Altitudes, J. Aviation Med. **11**:108-111, 1940.

At altitudes requiring the administration of oxygen a mask is worn which protects most of the face. Also, because of the painful glare it is necessary to employ goggle lenses or spectacle lenses which have been tinted so as considerably to reduce the total transmission of light. These glare-reducing protective lenses must, of course, comply with the same standards of optical measurement as any other good spectacle lenses. In aerial combat the goggles must also serve to protect the eyes against flash and against flying bits of metal.

Many problems still exist relative to goggles for flying. The ideal goggles for flying should possess the following characteristics:

1. They should afford adequate protection against glare, against air blast and against flying debris, dust and flash burn.

2. They should provide a totally unrestricted visual field for each eye. Goggles at present issued seriously restrict the nasal portion of each visual field.

3. They should be so designed as to integrate well with the upper portion of an oxygen mask and still fit snugly about the nose and the infra-orbital area when the oxygen mask is not being worn.

4. They should afford maximum comfort.

5. They should be so ventilated as to be free from fogging or frosting.

6. They should contain no metal or shatterable glass to cause ocular or orbital injury on crash landings.

7. Finally, they should be free from optical error.

Recently a type of goggles has been developed by the Aviation Section, Research Division of the Bureau of Medicine and Surgery, United States Navy Department, which approaches these requirements, and these are now being issued as alternate or optional equipment. With these goggles are supplied quickly interchangeable lenses of two colors and densities along with two extra clear lenses.

The pilot's and the gunner's vision are of the greatest importance in military flying. Workers in the field of aviation medicine must be concerned not only about such matters as the design for goggles but also about the design of the airplane itself in their efforts to provide the best possible vision for the flying personnel. The quality of clear plastic windshields, radomes and gunners' plastic enclosures are matters of vital concern. Much is being done to improve these mediums.

ABSTRACT OF DISCUSSION

DR. CONRAD BERENS, New York: Although there is little I can add to Captain Carson's splendid contribution, it is a privilege to discuss a paper on the subject of changes in atmospheric pressure as they affect ocular functions by a man who has had so much practical experience in this field. Because reference has been made to the fact that I worked in this field during the last war, it occurred to me that some historical points might be of interest, since much of the new information is secret.

When the United States entered the First World War, the only allusions to altitude in its relation to ocular functions referred to experiments in the low pressure chamber by the great French pioneer, Paul Bert, and others. Balloonists at times mentioned the difficulty of seeing the column of mercury in the barometer at high altitudes. Sometimes mountain climbers noticed a failure of vision or, more often, of accommodation. There was still some question of the exact cause for the physical and ocular disturbances produced by altitude, in spite of the excellent work of Henderson, Schneider, Haldane and Dwyer on Mount McKinley.

I was fortunate in having Drs. Schneider, Henderson and Dwyer to work with me in my original investigations. Our group, which included three members of this section, namely, Drs. Dunnington, Webster and Skeel, soon found that at the altitudes at which we worked, up to about 28,000 feet (9,000 meters) for most of the runs in the low pressure chamber or in the rebreathing apparatus, the administration of oxygen almost immediately restored ocular functions to normal, and that this occurred when the barometric pressure was held constant. In a paper published in 1918 we concluded that the lowered visual acuity, the lowered retinal sensitivity to white and to colored light, the contraction of the visual and binocular fields and the weakening of accommodation, convergence, divergence and supravergence were caused mainly by lack of oxygen and were not due to the many other suggested conditions, such as lowered blood pressure, decreased atmospheric pressure, carbon monoxide, nervous strain and vibration of the motor. In our experience, the administration of oxygen prevented the occurrence of the untoward symptoms, and when these symptoms occurred through its want oxygen quickly restored the functions to normal.

One of our records, made in 1918, of the effect of the administration of oxygen on convergence and accommodation while the atmospheric pressure was held constant at low level is shown in figure 1.

I am particularly interested in Captain Carson's discussion of altitude in flying and the relative infrequency of acute anoxic ocular symptoms. I understand that most of the bombing at night by British planes is done at about 20,000 feet (7,000 meters) and that a great deal of the bombing by American planes in daylight is done at 27,000 feet (9,000 meters) and lower. Therefore, only under the circumstances that Captain Carson cited will acute symptoms of aeroembolism arise. I have had no experience with the toxic effects of oxygen which he discussed.

His account of the effects of prolonged flights below 10,000 feet (3,300 meters) is most interesting, as we had already concluded from our original investigations that the eyes would be affected only by prolonged exposure to this altitude. In studying this type of flight it was hard to eliminate other factors which are now known to produce flying fatigue.

In the low pressure chamber we had no experience with aeroembolism, and the planes used in the first World War did not attain 35,000 feet (12,000 meters). Visual disturbances from aeroembolism are more com-

mon in the present conflict, but so far most of the changes reported have been transient. I have heard of 1 case, however, in which visual disturbances, presumably due to aeroembolism affecting the visual cortex, apparently persisted for several days.

The dazzling effect of excessive solar light has been recognized for many years. We studied the various types of goggles and glass which were most effective in preventing difficulties from this source. Certainly for flying over snow and water and into the sun, lenses which effectively reduce the incident light are necessary, and it is also desirable to have lenses which disturb color values as little as possible. The problem today is different from that in the last war, when airplanes had open cockpits.

One new angle is the question of contact lenses. Commander Nichols of the Royal Canadian Air Force told me the other day that contact glasses greatly reduce efficiency in flying at night and cause troublesome dazzling in landing and in flying into the sun. On the other hand, I know of one successful navy combat pilot who seems to have had no difficulty and who has made a splendid combat record.

I wish Captain Carson would discuss the effects of acceleration and deceleration and of "blacking out" and "redding out," because the increasing speed of planes, especially with the new propulsion types of motors, will bring this problem more and more to the fore.

CAPTAIN LEON D. CARSON: The review by Dr. Berens of the facts of historical interest to flight surgeons is a little startling each time I hear it. The work of the men who did research in this field in the past is so closely parallel to the problems which are now of current interest as to indicate what a careful study and appraisal was made of the problems as they existed at that time, problems which still exist. Of course, back in 1916, 1917 and 1918 "blackout" was not a common problem in flying, since the planes were able to withstand less stress than the pilots who flew them.

There are two types of acceleration that produce stress in military aircraft. These are linear acceleration and acceleration in the vertical axis of the pilot (centrifugal acceleration). Linear acceleration may not be of a high order in starting and stopping except in cases of catapult shots and crash landings. A great deal has been done to negate the effects of linear acceleration both in crash landings and in dogfights. The development of the jet propulsion or rocket propulsion aircraft we have been reading about in the papers is going to add to our problems in this field of acceleration. Acceleration is a function of the square of the velocity divided by the radius of the curve through which an airplane flies. If a pilot flies an airplane around a certain arc at a given speed, he may, by means of accelerometers, determine the multiple of g, or gravitational force, that is stressing every structure of that moving plane, as well as every structure of himself. If he doubles the speed of the airplane, that is, halves the time of its flying around a given circle, he is doubling the acceleration twice (that is, 2 squared, or 4 times the amount of g). It has been determined that the human body can stand relatively high gravitational or accelerative loads provided these stresses are not applied for more than about three seconds at a time. The upper limit of tolerance for gravitational stress seems to be about 4 or 4½ g's if stress is maintained during a standard interval of five seconds. As this value of g is exceeded, more and more pilots are blacked out. There is a rather wide range of tolerance in the human being in his response to accelerative stress. Henderson, in a very good article, which was republished in *Science* two years ago and which was a review of his article on the venopressor mechanism, gave a pretty fair clue as to what is going on in the case of pilot's blackout. There is no doubt that the pilot has pooling of the blood below the level of the heart and that this pooling of blood takes place in the dependent portions of the body, the extremities, the abdomen, the arms and the legs. If a means can be found to protect those dependent portions of the body against engorgement due to the effects of the strong accelerative forces on the column of blood the human tolerance for that type of stress can, theoretically, be considerably increased. Without going into the question of how this is done, which of course is not a matter for free discussion at the moment, I may say that there have now been used in actual flight in this country, in Australia and in Great Britain three different types of supportive devices which have been adapted to use in airplanes and which have been found to raise the average tolerance of human beings by a matter of from 2½ to 2¾ g. When it is calculated in terms of actual weight that if a man weighs 150 pounds (68 Kg.) and a force of 6 g is applied he bears down on his feet with 6 times 150 pounds, or 900 pounds (408 Kg.), it is seen that 2½ × 150 pounds is a considerable increment of weight. Experiments in this connection are still going on. The Canadians have developed a huge human centrifuge and a complete biophysical laboratory, and also a fine library to go with it, and the Mayo Aeronautical Laboratory has done similarly. A new human centrifuge has been installed at Wright Field, and some interesting tests are being made at Pensacola, Fla.. A great deal of time could be consumed in telling what tests are made in these centrifuge runs, but I am afraid lack of time will prevent a more general discussion.

HERPES SIMPLEX KERATITIS IN MALARIA

CLINICAL AND EXPERIMENTAL STUDY

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During recent months increasing numbers of otherwise healthy troops have contracted malaria in tropical combat areas. In these patients numerous instances of keratitis due to herpes simplex virus have been encountered. These infections have frequently resulted in serious scarring of the cornea, and the ulcers have been prone to recur with successive attacks of malaria. For these reasons it has seemed worth while to consider the relation between malarial fever and herpetic keratitis.

The most common corneal lesion of herpes simplex is an epithelial infection which is usually seen as an irregular linear ulceration with characteristic dendritic contour. Multiple discrete superficial punctate lesions may be found alone or simultaneously with a dendritic ulcer. Deep keratitis may develop from a preexisting superficial lesion or may appear as a disciform keratitis involving primarily the corneal parenchyma. A disturbing feature is the recurrence of small rounded metaherpetic ulcers. Corneal hypesthesia is characteristic of all these manifestations. Instances of every variety of herpes simplex keratitis have been encountered in patients with recurrent malarial attacks, but this paper is chiefly concerned with superficial dendritic keratitis.

Horner [1] in 1871 first described the dendritic ulcer as a morphologic entity and on clinical grounds suggested a possible relationship with lesions due to herpes elsewhere on the body.

In the years that followed, a number of clinicians were impressed with the frequency of this type of ulceration in malarial fever (Kipp [2] 1880 and 1889, Wilder [3] 1893, Ellett [4] 1899, Charles [5] 1904). In the first world war large numbers of British troops were infected with malaria, and a number of cases of dendritic keratitis were reported (Kiep,[6] Maxwell,[7] Bywater [8]).

Because of the frequent association in onset of corneal ulcers and malarial attacks, some reports ascribed the ulcers strictly to malaria (Kipp [2] 1880-1889, Ellett [4] 1899, Charles [5] 1904, Kiep [6] 1922, Bywater [8] 1922). However, an increasing number of publications supported Horner's original contention that they were probably a manifestation of herpes simplex (Hagnauer [9] 1891, Wilder [3] 1893, Maxwell [7] 1918). In discussing the question of keratitis in malaria, R. H. Elliot [10] in his treatise "Tropical Ophthalmology" maintained a judicious attitude of skepticism in making the observations that while (1) there is an obvious association between malaria and this form of corneal ulceration, (2) the keratitis cannot be regarded as purely a manifestation of plasmodial disease.

Grüter [11] in 1920 first reported the existence of a specific virus in the fluid of corneal herpes simplex vesicles and showed that the disease can be transferred to the cornea of a rabbit. He likewise confirmed the common theories of the causation of the different lesions produced by this virus in the eye and about the face or the genitalia.

Extensive research has been devoted to the herpes simplex virus and also to the relation of this organism to the eye. The outstanding study

1. Horner, F.: Ueber Herpes cornealis, Klin. Monatsbl. f. Augenh. **9**:321, 1871.

2. Kipp, C. J.: On Keratitis from Malarial Fever, Tr. Am. Ophth. Soc. **3**:91, 1880; Further Observations on Malarial Keratitis, ibid. **5**:331, 1889.

3. Wilder, W. H.: Dendritic Keratitis, J. A. M. A. **21**:604 (Oct. 21) 1893.

4. Ellett, E. C.: A Series of Cases of Malarial Keratitis with a Report of Blood Examinations, Ophth. Rec. **8**:115, 1899.

5. Charles, T. W.: Dendritic Keratitis, Am. J. Ophth. **21**:97, 1904.

6. Kiep, W. H.: Ocular Complications Occurring in Malaria, Tr. Ophth. Soc. U. Kingdom **42**:394, 1922.

7. Maxwell, E. M.: Observations on Eye Conditions Met with in Malta, 1916-17 (Occurring Among British Troops in the Balkans and Malta Garrison), Brit. J. Ophth. **2**:406, 1918.

8. Bywater, H. H.: Notes on Malarial Conditions of the Eyes, Tr. Ophth. Soc. U. Kingdom **42**:359, 1922.

9. Hagnauer, E.: Ueber die Misdeutungen des Herpes corneae febrilis, Zurich, Hofer & Burger, 1891; cited by Wilder.[3]

10. Elliot, R. H.: Tropical Ophthalmology, London, Oxford University Press, 1920, p. 453.

11. Grüter, W.: Experimentelle und klinische Untersuchungen über den sogenannten Herpes corneae, Klin. Monatsbl. f. Augenh. **65**:398, 1920.

on ocular herpes has been that of Gundersen,[12] in Boston. The present status of knowledge in this field has been recently summarized by Thygeson[13] in his monograph "Viruses and Virus Diseases of the Eye."

Since the definitive establishment of the virus causation of dendritic keratitis there have been occasional references to an association with malaria. Finnoff[14] reported 2 instances of dendritic keratitis occurring in therapeutic malaria and suggested the danger of inducing herpetic keratitis when employing malarial fever therapy for syphilis of the central nervous system. Post[15] and Lloyd[16] have observed that there is an apparent correlation between malaria and dendritic ulceration. Gundersen[12] recorded 1 case of malaria, and he found that the majority of the dendritic ulcers in his extensive series were associated with infections of the upper respiratory tract. Duke-Elder[17] has listed influenza and pneumonia as febrile conditions frequently associated with herpetic keratitis. Berliner[18] reported an instance of dendritic ulcer following artificial pyrexia induced by diathermy, while Finnoff[14] and Lloyd[16] mentioned foreign protein shock therapy as a precipitating factor. That fever alone does not often precipitate dendritic keratitis is evident from the fact that Solomon,[19] working under Stecher at Cleveland City Hospital, did not encounter a single instance of this corneal compilation in 10,000 treatments in the fever cabinet.

INCIDENCE OF HERPES KERATITIS IN MALARIA

Because of the apparent frequency with which the onset of herpes simplex keratitis has been chronologically associated with acute recurrences of malaria, it was decided to investigate the incidence of this type of corneal infection among malarial and among nonmalarial patients.

The new patients examined in the clinic with which we have been associated during an eighteen month period fall into two comparable groups. The first had been in a malarial district under combat conditions for four months and had a malarial incidence of about 80 per cent, but the patients were otherwise in good physical condition. The second was composed of troops free from malaria. The two divisions lived under similar camp conditions in an area where minor infections of the respiratory tract are common but primary infection with malaria is unknown.

Table 1 indicates the incidence of various types of keratitis in these two groups.

TABLE 1.—*Incidence of Various Types of Keratitis Among New Eye Clinic Patients Derived: (1) From Troops Exposed to Malaria and (2) From Troops Not Exposed to Malaria*

	I Troops Exposed to Malaria	II Troops Not Exposed to Malaria
Total number of new patients	2,448	2,200
Superficial herpes simplex keratitis	13	2
Catarrhal ulcers	14	6
Interstitial keratitis	1	1
Meningococcic ulcer	0	1
Herpes zoster keratitis	1	1

Plasmodium vivax (the causative agent of benign tertian malarial fever) was demonstrated in blood smears from all 13 patients who had keratitis associated with herpes simplex and who had been exposed to malaria. In each patient the onset of corneal ulceration followed shortly an acute malarial recurrence. None of these patients had concomitant infections of the respiratory tract. In this limited series the incidence of dendritic keratitis in the malarial group was 1 in each 188 new patients examined in the ophthalmologic clinic, whereas among patients not exposed to malaria the incidence was 1 in each 1,100 new patients. Hence corneal infection associated with herpes simplex would seem to be about six times as frequent among troops infected with malaria. However, it is significant that only a fraction of 1 per cent of the patients admitted to the hospital with malaria ever contracted herpetic keratitis. In this study the incidence of keratitis associated with herpes simplex among new patients with acute recurrent malaria admitted to the general medical service of this hospital was less than 0.2 per cent, or about 1 in 700 patients. Although keratitis associated with herpes simplex is much more frequently encountered in a population heavily infected with malaria, the percentage of patients

12. Gundersen, T.: Herpes Corneae, with Special Reference to Its Treatment with Strong Solution of Iodine, Arch. Ophth. **15**:225 (Feb.) 1936.

13. Thygeson, P.: Viruses and Virus Diseases of the Eye: II. Viruses of Ocular Importance, Arch. Ophth. **29**:488 (March) 1943.

14. Finnoff, W. C.: Dendritic Keratitis Following Therapeutic Inoculation of Malaria, Am. J. Ophth. **12**: 978, 1929.

15. Post, M. H.: Dendritic Keratitis, Am. J. Ophth. **12**:884, 1929.

16. Lloyd, R. I.: Herpes and Allied Conditions, Am. J. Ophth. **14**:601, 1931.

17. Duke-Elder, W. S.: Textbook of Ophthalmology, London, Henry Kimpton, 1939, vol. 2, 1894.

18. Berliner, M. L.: Herpes Cornea Occurring After Artificial Hyperpyrexia Induced by Diathermy, Arch. Ophth. **10**:365 (Sept.) 1933.

19. Stecher, R. M., and Solomon, W. M.: Complications and Hazards of Fever Therapy: Analysis of 10,000 Consecutive Fever Treatments with Kettering Hypertherm, Ann. Int. Med. **10**:1014, 1937; personal communication to the authors.

with acute malaria that contract this type of keratitis remains small.

TREATMENT

The management of keratitis associated with herpes simplex in malaria must be founded on energetic treatment of the malarial fever. Recurrent attacks of malaria occur even under optimum conditions and are often accompanied by reactivation or extension of the dendritic ulcer. There is no specific treatment for herpes simplex of the cornea. The generally accepted routine attempts to destroy the infected epithelium either by cautery or by curettage. Common usage favors the employment of an alcoholic solution containing 7 per cent iodine and 5 per cent potassium iodide, and this has been recommended by Gundersen.[12] Local application of ether [20] has been suggested, and vitamin B_1 [21] has been advocated as beneficial in herpetic keratitis. Frank [22] has used herpes simplex vaccine, and Davis [23] spoke favorably of employment of smallpox vaccine. Schwartz [24] has recently emphasized the importance of removal of foci of infection in the treatment of herpes simplex corneae. No single procedure has met with uniform success.

Administration of sulfonamide compounds by mouth was favorably reported on by Kleefeld,[25] but, as Thygeson [13] has pointed out, there is no indication from animal experimentation that the virus of herpes simplex is susceptible to chemotherapy. However, it would seem possible that secondary infection might play a part in certain instances. Furthermore, Gundersen [12] found that the virus cannot be recovered from the recurring erosions of the metaherpetic type.

In view of the good results often obtained through therapy of nonherpetic ulcerative keratitis with sulfonamide compounds, it seemed worth while to attempt an evaluation of the local use of sulfanilamide or sulfadiazine in the treatment of dendritic keratitis. The powdered drug was applied twice daily to the corneal lesions. In some instances the use of a sulfonamide compound was combined with other forms of therapy. Atropine and local heat were employed in all instances, and foci of infection were eliminated when this procedure was indicated. There is considerable individual variation in the severity of dendritic ulcers and in their response to general therapy. For this reason the results of any specific treatment must be interpreted with caution.

REPORT OF CASES

CASE 1.—An 18 year old white youth was admitted to the hospital on June 14, 1943 with his third acute attack of malaria. A few hours after admission he complained of irritation, tearing and photophobia in the left eye. There was no history of a similar episode or of injury. His visual acuity was 20/20 in the right eye and 20/40 in the left. A superficial ulceration of dendritic pattern involved the temporal third of the cornea. A blood smear yielded Plasmodium vivax. A test of the skin with herpes simplex antigen gave strongly positive results. The patient's blood serum showed antibodies capable of protecting the chorioallantoic membrane against approximately 100,000 infectious units of known herpes simplex virus.

Sulfadiazine powder was applied to the lesion twice daily for six days, with complete healing of the ulcer. When the patient was discharged to full duty, vision in the affected eye had improved to 20/30. There had been no recurrence of keratitis after two months.

CASE 2.—A 27 year old white man was admitted to the hospital on May 26, 1943 with his first attack of malaria, approximately six months after leaving a malarious area. One day after admission he noticed irritation, tearing and photophobia in his left eye. There was no history of similar complaint or of injury. His visual acuity was 20/20 in the right eye and 20/20 in the left. Three discrete, irregular, star-shaped areas of superficial ulcerations were present in the pupillary area of the left eye. A blood smear yielded Plasmodium vivax. The patient was treated for two days with instillation of a 0.25 per cent solution of zinc sulfate and with mercury bichloride ointment 1:5,000, with no improvement. Sulfadiazine powder was then applied to the ulcer twice daily for thirteen days, with complete healing of the cornea. When the patient was discharged to full duty, vision was 20/20 in each eye. There had been no recurrence of keratitis in two months.

CASE 3.—A 33 year old white man was admitted to the hospital May 25, 1943 with his third attack of acute malaria. Within twenty-four hours of his admission he noticed increasing irritation, redness and tearing in his left eye. There was no history of a similar episode or of injury. Visual acuity was 20/20 in the right eye and 20/70 in the left. Examination showed a small dendritic ulceration in the center of the pupillary area of the left eye. The blood smear yielded Plasmodium vivax. A cutaneous test with herpes simplex antigen gave strongly positive results. The patient's blood serum showed antibodies capable of protecting the chorioallantoic egg membrane against approximately 100,000 infectious units of known herpes simplex virus.

For twenty-four hours a 0.25 per cent solution of zinc sulfate was instilled and mercury bichloride ointment 1:3,000 employed, without alteration in the lesion.

20. Kronenberg, B.: Treatment of Herpetic Keratitis with Ether, Arch. Ophth. **26**:247 (Aug.) 1941.

21. Nitzulescu, J., and Triandof, E.: Treatment of Herpetic Keratitis with Vitamin B, Brit. J. Ophth. **21**: 654, 1937.

22. Frank, S. B.: Formalized Herpes Virus Therapy and the Neutralizing Substance in Herpes Simplex, J. Invest. Dermat. **1**:267, 1938.

23. Davis, P. L.: Recurrent Herpes of the Cornea and Recurrent Herpetic Fever: Results of Treatment with Smallpox Vaccine, J. A. M. A. **114**:2098 (May 25) 1940.

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25. Kleefeld, G.: Traitement des affections herpétiques cornéennes et de l'ulcère dendritique par des dérivés sulfonamides, Bull. Soc. belge d'opht. **76**:14, 1938.

Sulfadiazine powder was then applied to the ulcer twice daily for eight days, with complete corneal healing. When the patient was discharged to duty there was a distinct central corneal scar; vision had improved to 20/50 in this eye. There was no recurrent ulceration, but the patient was seen two months later complaining of blurring and irritation, which were aggravated by exposure to glare and wind. These complaints were such as to interfere with full duty in the field, and assignment to limited duty was recommended.

CASE 4.—A 25 year old white man was referred to the ophthalmologic eye clinic on Feb. 19, 1943, while under treatment for his third attack of malaria. He complained of irritation, tearing and blurred vision in the right eye. There was a history of three similar episodes prior to his induction into military service. His visual acuity was 20/50 in the right eye and 20/20 in the left. An arborescent superficial scar involved the central and the temporal portion of the right cornea. There was a small irregular area of ulceration below the pupil. The blood smear yielded Plasmodium vivax. After treatment with atropine and local heat for one week the cornea was healed. On May 11, 1943 the patient suffered a fourth attack of malaria; three days later he complained again of irritation in the right eye. Examination showed a classic dendritic ulceration below the pupil. There were, in addition, a number of discrete elevated staining points, which consisted of small epithelial excrescences giving the appearance of filamentary keratitis.

On this occasion the eye was treated with sulfanilamide powder twice daily for five days, with only slight improvement. Therapy was then changed to local applications of sulfadiazine powder, and there was complete healing of the lesion in nine days. With vision impaired to 20/50 in the right eye, the patient was recommended for assignment to limited duty.

CASE 5.—A 22 year old white man was admitted to the hospital on Jan. 14, 1943 complaining of redness, irritation and severe photophobia in the left eye. The onset of the ocular complaint occurred two weeks prior to his admission and followed shortly an acute attack of malaria. There was no history of injury. The visual acuity was 20/20 in the right eye and 20/200 in the left. There was an irregular band of dendritic ulceration extending diagonally across the pupillary area. The blood smear yielded Plasmodium vivax. The patient showed no improvement when treated for two weeks with atropine and local heat. Strong solution of iodine U. S. P. was applied on two occasions without apparent benefit. Sulfanilamide powder was used twice daily for eight days with no improvement. The eye was then treated with sulfadiazine powder, and there was complete healing of the ulcer in eight days. During four months' observation, this patient had two more acute attacks of malaria, despite intensive courses of malarial therapy. With each attack of fever there was a reactivation of the keratitis. On the first occasion discrete superficial punctate lesions appeared in previously normal areas of the cornea, while with the second malarial attack there was a marked dendritic extension from the original site of ulceration. The vision in the affected eye remained 20/200, and the patient was recommended for assignment to limited duty.

CASE 6.—A 20 year old white man was admitted to the hospital on March 17, 1943 with his fourth attack of malaria and a complaint of redness, burning and tearing in the left eye. There was no history of a similar ocular complaint or of injury. The patient's vision was 20/20 in the right eye and 20/30 in the left. Examination disclosed a superficial ulceration of dendritic contour occupying the temporal inferior quadrant of the left eye. The blood smear yielded Plasmodium vivax. A cutaneous test with herpes simplex antigen gave strongly positive results. The patient's blood serum showed antibodies capable of protecting the chorioallantoic egg membrane against approximately 100,000 infectious units of known herpes simplex virus.

Instillations of 0.25 per cent zinc sulfate solution and mercury bichloride ointment 1 : 3,000 were used for two days without effect. Sulfanilamide powder was applied to the ulcer twice daily for six days with no improvement. The ulceration was then treated with strong iodine solution, with complete healing in six days. There was no recurrence of corneal erosion, and vision had improved to 20/20 when the patient was discharged to full duty. There had been no recurrence of keratitis after five months.

CASE 7.—A 24 year old white man was admitted to the hospital on Feb. 26, 1943 with his first attack of acute malaria. Four days later he noticed irritation, tearing and photophobia in the right eye. One year previously he had had a similar ocular complaint, which was not associated with malarial fever. His visual acuity was 20/30 in the right eye and 20/20 in the left. Examination showed a superficial corneal ulceration of dendritic pattern involving the inferior quadrant of the right eye. Plasmodium vivax was present in the blood smear. The ulcer was treated with strong solution of iodine and healed in three days, only to recur after one week. A second application of iodine to the recurrent ulceration was of no apparent benefit. Sulfadiazine powder was then applied to the ulcer twice daily for ten days, but without improvement. The lesion finally healed after two weeks' further treatment with 0.25 per cent zinc sulfate solution and mercury bichloride ointment 1 : 3,000. Vision in the affected eye remained 20/30. Despite having completed an intensive course of malarial therapy, the patient had a recurrent attack of acute malarial fever six weeks after admission.

Because of persisting irritation in the left eye aggravated by recurrent malaria, the patient was recommended for assignment to limited duty.

CASE 8.—A 22 year old white man was admitted to the hospital March 31, 1943 with his fourth attack of malaria. On the following day he noticed increasing irritation and tearing in the left eye. There was no history of injury, and the patient had had no previous ocular disorder. His visual acuity was 20/20 in the right eye and 20/20 in the left. Examination disclosed a dendritic ulceration involving the inferior quadrant of the left cornea and extending to the border of the pupillary area. A blood smear yielded Plasmodium vivax. A cutaneous test with herpes simplex antigen gave strongly positive results, and the patient's blood was found to contain antibodies capable of protecting the chorioallantoic membrane against 100,000 infectious units of known herpes simplex virus. The eye was treated with strong solution of iodine, with healing of the ulcer in four days, but epithelial erosions recurred at the site of the original lesion. To this secondary ulceration sulfadiazine powder was applied twice daily for three days without improvement. Administration of the drug was discontinued, as the patient was transferred for disciplinary action, and the exact date of healing was not known. Irritation subsided in about one week, and when the patient was examined one month later the cornea was completely healed. Vision was 20/20 in each eye, and the patient was performing full field duty without complaints. There had been no recurrence of keratitis after five months.

CASE 9.—An 18 year old white youth was admitted to the hospital with his second attack of malaria on Aug. 9, 1943. Two days later he noticed increasing redness and irritation of the left eye. There was no history of injury or of previous ocular complaint. His vision was 20/20 in the right eye and 20/30 in the left. Examination showed a superficial dendritic ulcer in the temporal inferior quadrant of the left cornea, encroaching on the pupillary area. Plasmodium vivax was present in the blood smear. A cutaneous test with herpes simplex antigen gave strongly positive results. Serum from the patient showed antibodies capable of protecting the chorioallantoic membrane against 100,000 infectious units of known herpes simplex virus. Curettings from the ulcer were transferred to a rabbit's cornea, where typical herpetic keratitis was apparent in forty-eight hours. After the initial curettage the patient was given atropine and local heat, and the cornea was healed in six days. However, two days later a small circular ulcer appeared at the original site. This ulcer was treated with sulfanilamide powder twice daily for seven days without improvement. Sulfadiazine powder was given in like manner for nine days with no benefit. The residual ulcer was then treated with strong iodine solution and healed in three days, but superficial erosions again recurred. Because of persistent irritation and failure of the cornea to heal permanently, the patient was evacuated after two months' treatment. The vision in the affected eye was reduced to 20/70.

CASE 10.—A 22 year old white man was admitted to the hospital on July 29, 1943 with his sixth attack of malaria. Five days later he noticed redness and irritation in the left eye. He gave a history of a similar episode of inflammation in this eye, which was associated with his first attack of malaria, ten months prior to his admission to the hospital. His visual acuity was 20/20 in the right eye and 20/200 in the left. Examination showed a band of dendritic ulceration extending from the upper limbus across the pupillary area, where it was continuous with a fascicle of vascularized superficial scar tissue running to the limbus below. A blood smear yielded Plasmodium vivax. A cutaneous test with herpes simplex antigen gave strongly positive results. Serum from the patient showed antibodies capable of protecting the chorioallantoic membrane against 100,000 infectious units of known herpes simplex virus. After the initial curettage the cornea was treated with sulfanilamide powder twice daily for ten days with no appreciable improvement. Curettings from the residual dendritiform ulcer were transferred to a rabbit's cornea. This resulted in establishment of typical herpetic keratitis. A more extensive curettement was then effected and sulfanilamide employed as before, the cornea healing in three days. However, a small circular erosion appeared after five days, and this lesion failed to respond to the powdered sulfanilamide. This secondary ulcer was finally curetted and healed in two days, but again there was a recurrence of epithelial erosion. Sulfadiazine powder was then employed twice daily for fourteen days, without benefit. After two months' treatment the patient was evacuated because of persisting irritation and impaired vision. At the time of transfer the visual acuity in the affected eye had improved to 20/50.

RESULTS OF TREATMENT WITH SULFADIAZINE

In 3 cases (cases 1, 2 and 3) there was prompt improvement with the use of sulfadiazine powder alone, the ulcers healing completely in six to fourteen days. In case 4, in which sulfanilamide had first been administered without apparent effect, the ulcer healed with nine days of local treatment with sulfadiazine. In case 5 sulfanilamide powder given for eight days was without effect, and two applications of strong iodine solution failed to result in complete healing. This ulcer finally healed solidly after eight days' local therapy with sulfadiazine. In case 7 a recurrent ulceration was treated with sulfadiazine for ten days without improvement. The ulcer in case 8 was treated with iodine and healed in three days, only to recur subsequently. This secondary erosion was treated with sulfadiazine for three days without apparent benefit. In case 9 a recurrent ulcer failed to heal after nine days' local therapy with sulfadiazine, and in case 10 a similar lesion showed no improvement after fourteen days' employment of the drug.

Thus in the 5 cases of ulcers of dendritic pattern, sulfadiazine was apparently helpful. However, there was no appreciable benefit which could be attributed to sulfadiazine in 4 cases of recurrent corneal ulcerations of the metaherpetic type.

RESULTS OF TREATMENT WITH SULFANILAMIDE

In cases 4, 5 and 6 the sulfanilamide powder was found to be of no benefit in treating fresh dendritic ulcers. In case 9 a recurrent ulceration was treated for seven days without apparent improvement. In case 10 sulfanilamide was apparently of no value even when combined with curettage. In this instance it was possible to demonstrate the presence of herpes simplex virus in the residual dendritic lesion after ten days' treatment with the powdered drug.

HERPES SIMPLEX KERATITIS AS A FACTOR INCAPACITATING TROOPS FOR FULL DUTY

Only in corneal infections does herpes simplex result in permanent scarring. The number of patients requiring assignment to limited duty because of impaired vision is notoriously high after attacks of dendritic keratitis, particularly when early and energetic treatment is not available. There is also the problem of ulceration recurring with subsequent attacks of malaria. Even without active erosion of the epithelium, the eye often remains irritable and sensitive to wind and glare for a long period.

In addition to the 13 patients with dendritic keratitis considered in determining the incidence among new patients coming to the clinic from malarial and nonmalarial groups, 7 patients with

active or recently healed superficial herpes simplex keratitis were transferred to this hospital from other areas. There were also 2 patients with nonspecific deep keratitis that was probably of the same causation. Of these 22 patients with dendritic keratitis, 15 could not be discharged to full duty and each of the 2 patients with deep keratitis of probable herpetic causation required evacuation. Table 2 shows the relative incidence of herpetic keratitis as a factor in restricting disposition of patients to full duty.

TABLE 2.—*Relative Incidence of Herpes Simplex Keratitis as Cause for Disposition to Limited Duty*

	No. Cases
Herpes simplex keratitis, superficial	15
Deep keratitis, probably herpetic	2
Sclerokeratitis	1
Interstitial keratitis, syphilitic	3
Trachoma	1
Inflammation of iris or choroid and retina	12
Ocular injuries	12

As may be seen, keratitis associated with herpes simplex necessitated more dispositions to limited service at this station during this period than any other single inflammatory lesion of the eye and also more than did ocular injuries.

LABORATORY TESTS

Transference of the Infection to the Cornea of Rabbits.—From a cornea of each of 2 patients with dendritic keratitis occurring in conjunction with acute malaria the virus of herpes simplex was isolated (cases 9 and 10). By the method described by Grüter,[11] scrapings were transferred directly to a cornea of a rabbit. In each instance typical herpetic keratitis was produced, and it was possible to transfer the infection to a cornea of a second rabbit.

Unfiltered exudate from the conjunctival cul-de-sac of the rabbit was then inoculated onto the chorioallantoic membrane of a 12 day chick embryo, according to the technic of Burnet.[26] The lesions produced were identical with those caused by a known strain (HFE) of herpes simplex virus.

To prove conclusively that the keratitis in the rabbits was due to herpes simplex virus, neutralization tests were carried out on successive samples of each animal serum. The first sample of blood was withdrawn at the time of the initial corneal infection. After inactivation at 56 C. for thirty minutes the serum was preserved at 4 C. A second specimen was taken after three weeks and was similarly treated. Simultaneous neutralization tests were then carried out according to the following technic:

A suspension of a known strain (HFE) of herpes simplex virus was used, containing approximately 100,000 infectious units as shown by a previous titration. This was added to an equal volume of the affected rabbit's serum, and 0.05 cc. of the mixture was then inoculated onto the chorioallantoic membrane of a 12 day chick embryo. After three days' incubation the eggs were examined. Serum from the first specimen taken at the time of the initial infection had failed to neutralize the virus. These membranes showed characteritic semiconfluent herpetic lesions, and in most instances the embryos were dead. However, the serum obtained three weeks after the initial infection completely neutralized the suspension of known herpes virus inasmuch as all embryos were living and there were no lesions due to the virus on the chorioallantoic membranes. It was therefore concluded that the causative agent which was isolated from the human cornea and was transferred to the rabbit's cornea and then to the chorioallantoic membrane of a 12 day chick embryo was herpes simplex virus.

Similar neutralization tests were carried out on the serums of 10 patients with active or recently healed dendritic keratitis. In each patient's serum antibodies were present which were capable of protecting the chorioallantoic membrane against about 100,000 infectious units of a suspension of known herpes simplex virus.

CUTANEOUS TEST FOR HERPES SIMPLEX INFECTION

Nagler[27] has described a specific cutaneous reaction present in persons infected with the virus of herpes simplex. He found a close correlation between positive cutaneous responses and presence of serum antibodies. It has been generally assumed that demonstration of serum antibodies is conclusive proof of past or present herpetic infection. Gallardo[28] has demonstrated, however, that absence of serum antibodies can occur during the first eighteen days of a keratitis which constitutes the primary lesion due to herpes simplex.

The herpes simplex antigen used in the cutaneous test consisted of heat-killed virus prepared from chorioallantoic membrane infected with the HFE strain of herpes simplex. The control was prepared from normal chorioallantois in a similar manner. An intradermal injection of 0.10 cc. was given, as in tuberculin tests, and readings were made after twenty-four hours.

The skin of 13 patients with active or recently healed herpetic keratitis was tested and in every instance found to give a strongly positive response to the antigen. Each of these patients had previously been shown by neutralization tests to have herpes simplex antibodies in the serum. Burnet and his associates[29] have re-

26. Burnet, F. M.: The Use of the Developing Egg in Virus Research, Medical Research Council, Special Report Series, no. 220, London, His Majesty's Stationery Office, 1936.

27. Nagler, F. P. O.: A Specific Skin Reaction in Persons Infected with the Virus of Herpes Simplex, to be published.

28. Gallardo, E. G.: Primary Herpes Simplex Keratitis: Clinical and Experimental Study, Arch. Ophth. **30**:217 (Aug.) 1943.

29. (*a*) Burnet, F. M., and Williams, S. W.: Herpes Simplex: New Point of View, M. J. Australia **1**:637, 1939. (*b*) Burnet, F. M., and Lush, D.: Herpes Simplex: Studies on Antibody Content of Human Sera, Lancet :629, 1939.

ported antibodies for herpes simplex virus present in as high as 90 per cent of adults. Using the cutaneous test, Nagler [27] found 80 per cent positive reactions among the older age groups. As a check on the incidence of positive cutaneous reactions in this hospital, the skin of 148 patients was tested as a sample. Of this total, 64 had had malaria and 84 gave no history of the disease. The incidence of positive cutaneous reactions was 78.1 per cent in the malarial group and 80.9 per cent in the nonmalarial group. The significance of a positive cutaneous reaction as an aid in the diagnosis of atypical keratitis in adults is therefore negligible, but a negative cutaneous reaction might prove valuable in ruling out herpetic infection of appreciable duration. Nagler,[27] however, in testing infants and young children found that the incidence of positive cutaneous reactions is less than 20 per cent in the first four years of life. Burnet and Lush [29b] have made this same observation on the basis of determinations of serum antibody, using the chorioallantois. The age distribution is likewise in accord with the following figures, quoted by Weyer,[30] for positive findings as to the presence of serum antibody: 0.5 years, 14 per cent; 5-10 years, 38 per cent. As Gundersen [12] has pointed out, it is this period, the first five years of life, that also has the highest incidence of dendritic keratitis. He further states that in young children herpetic keratitis is frequently mistaken for interstitial keratitis or phlyctenulosis. In such cases an easily repeated cutaneous test could prove of value, particularly when detailed examination is difficult and extensive laboratory facilities are not available.

SUMMARY AND CONCLUSIONS

There appears to be an increased incidence of keratitis associated with herpes simplex in a population heavily infected with malaria. Among new patients at the ophthalmologic clinic studied during an eighteen month period, there have been more than six times as many from a malarial division as from a comparable group that had not been exposed to malaria. However, less than 0.2 per cent of patients with acute malaria admitted to the general medical service of this hospital ever had this type of herpetic keratitis. Hence the likelihood of precipitating a dendritic ulcer in the individual patient with therapeutic malaria would seem very small.

Early diagnosis and intensive treatment of the malarial fever are essential in the management of herpetic keratitis occurring in patients with malaria. Recurrent attacks of malaria are often associated with a reactivation or an extension of the corneal ulceration.

Through impairment of vision and prolonged irritation of the eye herpes simplex keratitis has necessitated more disposition to limited duty of patients at this station than any other single eye condition.

Sulfadiazine powder applied locally to 5 dendritic ulcers seemed to promote rapid healing in each instance. In 4 cases of atypical recurrent herpetic ulcers sulfadiazine was of no demonstrable benefit. These results suggest that sulfadiazine may prove a satisfactory adjunct to the accepted treatment of dendritic keratitis with strong solution of iodine U. S. P.

Local applications of sulfanilamide were of no apparent value. In 3 patients with ulcers of dendritic pattern and in 1 patient with recurrent ulceration no improvement resulted. The herpes simplex virus was isolated from 1 dendritic ulcer after ten days' treatment with the drug.

From the cornea of each of 2 patients with recurrent malarial attacks and dendritic keratitis the causative agent was transferred to a rabbit's cornea and thence to the chorioallantoic membrane of a chick embryo, where characteristic lesions of herpes simplex virus were produced. The identity of the virus was confirmed by neutralization tests.

When the skin was tested for sensitivity to herpes simplex antigen positive responses were obtained in about 80 per cent of a sample of hospitalized adult patients, and there was no appreciable difference in incidence between malarial and nonmalarial patients.

Thirteen patients with herpes simplex keratitis were shown by neutralization tests to have serum antibodies against a known strain of herpes simplex virus. Each of these patients gave a strongly positive cutaneous reaction to the herpes simplex antigen.

The possible value of such a cutaneous test in certain atypical cases of herpetic keratitis has been indicated.

We received advice regarding this work from Dr. F. M. Burnet. Dr. Burnet also made available the laboratory facilities of the Walter and Eliza Hall Institute of Research in Pathology and Medicine, Melbourne, Australia.

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TOXOPLASMOSIS

REPORT OF OCULAR FINDINGS IN INFANT TWINS

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DETROIT

Toxoplasmosis is a recently recognized infectious disease in human beings. Four principal types have been reported: (1) a granulomatous encephalitis, usually of congenital origin and occurring in fetal or early infantile life; (2) an acquired acute encephalitis occurring in children; (3) an acquired acute disease resembling Rocky Mountain spotted fever occurring in adults; (4) a latent subclinical form occurring in adults.

Sabin, in 1943,[1] outlined the status of Toxoplasma, which was isolated by Nicolle and Manceaux from the gondi North African rodent in 1908 [2] and by Splendore from the rabbit in Brazil in the same year. The parasite has been classified as a protozoon of the genus Toxoplasma. It has a wide geographic distribution and occurs in many species of animals, both wild and domestic. Sabin and Olitsky in 1937 [3] found the parasite in guinea pigs and were able to transmit it through several animal passages. The morphologic characteristics of Toxoplasma have now been well established by Perrin,[4] and the features of the experimental disease have been studied adequately by Levaditi,[5] Sabin [6] and Wolf, Cowen and Paige.[7] Little is known about the life cycle of Toxoplasma, the natural mode of transmission and the epidemiology of human toxoplasmosis.

In infants the central nervous system is especially susceptible to toxoplasmic infection. The principal clinical findings are internal hydrocephalus or microcephaly, roentgenographic evidence of focal cerebral calcifications and bilateral chorioretinitis, which attacks particularly the area centralis. Convulsions are commonly noted. The spinal fluid in the active stage of the disease shows an increase in protein content, pleocytosis and xanthochromia. Additional diagnostic evidence may be obtained by demonstration of neutralizing antibodies against Toxoplasma in the serum of the patient. The technic was developed by Sabin [8] and consists in mixing varying dilutions of the patient's serum with a suspension of mouse brain containing the parasites and injecting the mixture intracutaneously into rabbits. The local reaction is compared with that produced by a similar mixture containing control serum from a normal person. The test is difficult to perform and even more difficult to interpret, but in trained hands it has given reliable results. In some cases it has been possible to transmit the disease to animals by inoculation of spinal fluid or tissues intracerebrally or intraperitoneally. The pathologic lesion in the central nervous system consists of necrosis followed by calcification and by a tendency to form granulomas. Miliary granulomas with epithelioid cells, focal meningeal and cerebral inflammatory areas with

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2. Nicolle, C., and Manceaux, L.: Sur un protozoaire nouveau du Gondi, Compt. rend. Acad. d. sc. **148**:369-372, 1909; Toxoplasma, Arch. Inst. Pasteur de Tunis **2**:97, 1909.

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4. Perrin, T. L.: Toxoplasma and Encephalitozoon in Spontaneous and in Experimental Infections of Animals, Arch. Path. **36**:568-578 (Dec.) 1943.

5. Levaditi, C.: Au sujet de certaines protozooses héréditaires humaines a localisations oculair et nerveuse, Compt. rend. Soc. de biol. **98**:297-299, 1928.

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7. Wolf, A.; Cowen, D., and Paige, B. H.: (*a*) Human Toxoplasmosis: Occurrence in Infants as an Encephalomyelitis; Verification by Transmission to Animals, Science **89**:226-277 (March 10) 1939; (*b*) Toxoplasmic Encephalomyelitis: III. A New Case of Granulomatous Encephalomyelitis Due to a Protozoon, Am. J. Path. **15**:657-694 (Nov.) 1939.

8. (*a*) Sabin, A. B., and Ruchman, I.: Characteristics of the Toxoplasma Neutralizing Antibody, Proc. Soc. Exper. Biol. & Med. **51**:1-6 (Oct.) 1942. (*b*) Sabin, A. B.: Toxoplasma Neutralizing Antibody in Human Beings and Morbid Conditions Associated with It, ibid. **51**:6-10 (Oct.) 1942.

lymphocytes, plasma cells, glial cells, large mononuclear cells, histiocytes, eosinophils and some capillary hypertrophy and conglomerate foci of necrosis, ranging from microscopic dimensions to several centimeters in size, are scattered through the hemisphere and into the white matter; cavities may be formed; parasites, intracellular and free, may be seen in affected or clear areas. Calcium forms early and is characteristically present in older lesions.[9] This substance appears on roentgenographic films as a few to many small rounded areas or curved lines, the latter of which are often seen in the basal ganglions. Internal hydrocephalus and large areas of cortical atrophy are commonly noted. Steiner and Kaump,[10] in a recent report on the pathologic changes in an infant, expressed the opinion that the lesions are pathognomonic. The ocular changes have been studied by Koch, Wolf, Cowen and Paige.[11] Adequate studies of the eyes in older patients were not found in the literature.

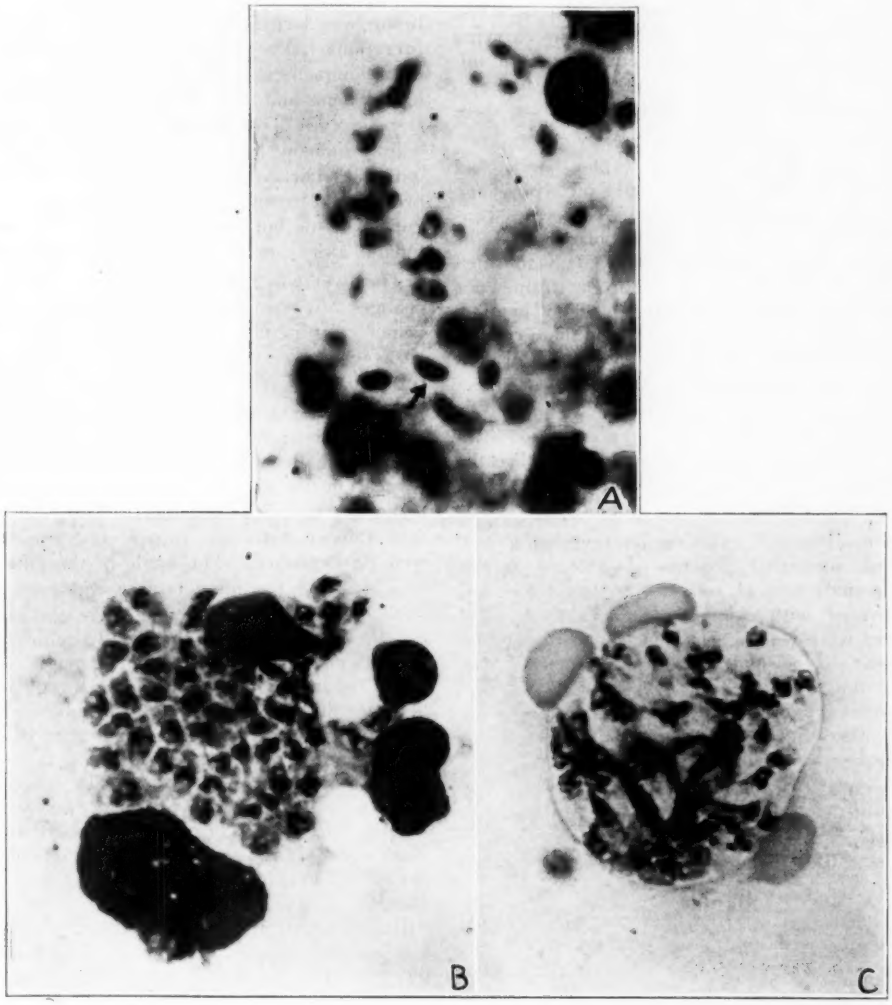

Fig. 1 (from Sabin[1]).—*A*, toxoplasmas in tissue after fixation in a dilute concentration of solution of formaldehyde U. S. P. Hematoxylin and eosin stain; × 1,400. *B*, intracellular aggregate of toxoplasma; × 1,000. *C*, pseudocyst; × 1,000.

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SUMMARY OF CASE HISTORIES [12]

CASE 1.—*History.*—H., a Negro premature infant and one of identical twins, was born on Sept. 5, 1943 and admitted to Children's Hospital half an hour after birth.

The mother had been in good health during pregnancy but during the last three months had complained of anorexia, attacks of dizziness and blurring of vision. Her blood pressure was said to have been normal. The expected date of confinement was October 17. There was no known cause for the premature onset of labor. The mother had not been aware that she was carrying twins. She had thought that the fetus had been unusually quiet during the last few months. She had two older children, aged 4 and 2 years, both of whom were in good health.

The father was likewise healthy. The family had come to Detroit in 1940 from the state of Mississippi. The father was a municipal employee, whose work consisted of collecting refuse. In the performance of his duties he had to handle dead rats, as well as to catch live ones. The family lived in a five room framework house in the Negro section of Detroit. They kept no pet animals, and the mother recalled no intimate contact with animals at any time. However, the house had been infested by mice at various times.

The patient was born by frank breech delivery five minutes after the other twin. He was extracted with difficulty and had to be stimulated in order to breathe and cry properly. Nevertheless, he had satisfactory color when he was admitted to the hospital.

Examination.—Physical examination revealed a well developed but somewhat inactive premature infant, weighing 3 pounds and 11 ounces (1,619 Gm.). The skin was covered with orange vernix caseosa. The cranial sutures were widely separated, but the fontanels did not appear to be under abnormal tension. The remainder of the findings were noncontributory. The laboratory data obtained on the child's admission to the hospital were likewise not unusual. The Kline test gave negative results.

Roentgenograms revealed slight enlargement of the heart and adequate aeration of the lungs. In the long bones, multiple transverse bands of increased density were noted near the metaphyses. The skull was not examined.

Course.—The patient received the usual care for premature infants. On the third day icterus of the skin and scleras was noted. There was also a transient fine punctate rash over the entire body. The icterus persisted, and abdominal distention developed. The stools became clay colored. The temperature was unstable, at first often subnormal and later febrile. There were repeated attacks of cyanosis. During one of these attacks the child died, at the age of 1 month.

Pathologic Study.—A complete autopsy was performed twelve hours after death. The pertinent gross somatic changes of significance were generalized icterus and enlargement of the liver and spleen. The brain presented a striking appearance, with numerous bright yellow lesions of varying size on the surface of the hemispheres. There was a severe degree of internal hydrocephalus. On the cut surface numerous cavities were noted. These were filled with gritty or friable yellow or white material, had irregular contours and often measured several centimeters in diameter. Similar yellowish material was present in the lining of the lateral ventricles.

Microscopically the cerebral lesions consisted of large areas of necrosis and calcification, which were often surrounded by granulation tissues composed of fibroblasts, histiocytes, giant cells, plasma cells and rare eosinophils. There were large, bandlike areas of calcification in the walls of the ventricles. The ependymal lining was largely destroyed and covered by glial proliferations. The vessels were surrounded by collars of inflammatory cells; in many areas, notably in the brain stem and the spinal cord, miliary granulomas were seen. These consisted of inflammatory cells, mainly mononuclear cells and glial elements. Parasites with the characteristic appearance of toxoplasmas were present in round, cystlike aggregates in apparently normal tissue but were seldom noted in areas of severe inflammatory reaction, necrosis or calcification.

The liver was the seat of diffuse, severe degenerative changes. There was fairly extensive extramedullary hemopoiesis in the liver, spleen and other organs. No parasites were found outside the brain, spinal cord and retina.

The right eye was removed and fixed entire in Zenker's solution; no gross abnormality was noted. The size was smaller than is normal for a full term baby. The corneal curve was less differentiated, more like that of an eye in a 7 month fetus. The sclera was a good deal thinner than the cornea, but episclera could be well distinguished. The angle of the anterior chamber was shallow; the mesoderm in the angle was not entirely atrophic (as it should be by the eighth month), and the remnants were abnormally cellular. Schlemm's canal was situated deep in the angle (fetal). The scleral spur, also, was behind the angle, as it should be into the seventh month. Red cells were in the anterior chamber. The major circle of the iris lay well behind the angle. (In an adult it is only slightly behind or on a level with it.) The sphincteric portion of the musculature of the iris was well developed (fourth month). The pupillary area showed a persistent vascular blood-containing fetal membrane and partly inflammatory remnants, some of which were attached to the capsule of the lens, as seen in fetal iritis. The stroma of the iris was loose, edematous and negroid. Increased pigment was noted in the anterior portion of the stroma, due to migration from a deep layer. The two pigment layers of the retina were edematous. The ciliary body was loose edematous and well developed with meridional muscle fibers, unlike the not clearly differentiated circular fibers (as should be the case in the seventh month). The ciliary processes were well developed, were loose and open and showed dissociation of pigment, plasma cell infiltration and a few nucleated erythrocytes. On the surface of the processes were noted a few plasma cells and monocytes, considerable tertiary vitreous and condensation of the *faisceau isthmique* and clumps of pigment. The pars plana was well developed, and the ora serrata was well behind the ciliary body. The conjunctiva near the limbus showed a few small foci of perivascular lymphocytes. The extraocular muscles at their attachment to the globe showed a few thin foci of lymphocytes and plasma cells. The lens, which was round, showed the epithelium of the anterior and posterior surfaces to be well developed. No retrolental

12. A full report on these 2 cases will be given in a separate article, which is now being prepared by one of us.

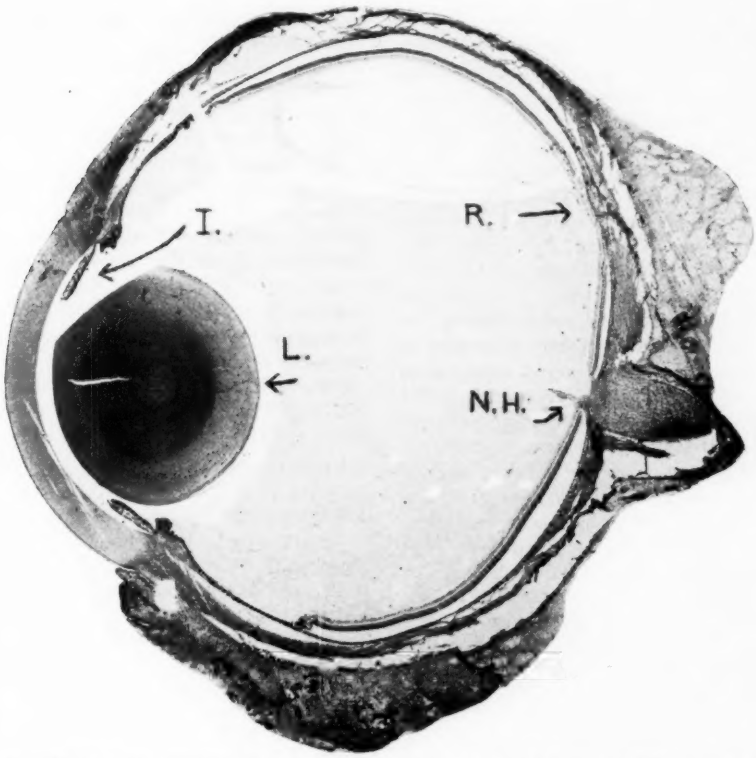

Fig. 2 (Case 1).—Horizontal section of the right eye. *I*, fetal iris and angle; *L*, fetal lens; *N.H.*, optic nerve head with persistent hyaloid artery; *R.*, chorioretinal lesion.

Fig. 3.—Details of the iris. *C*, cornea; *I*, iris; *V.M.*, vascular membrane; *L*, lens with rèmnant of adhesion.

vessels were seen. The vitreous was coarsely fibrillar and contained a few cells—mostly large mononuclears.

The choroid was well differentiated but more cellular than that of an adult. It showed extensive involvement, with rather sharply bordered destructive granulomatous lesions accompanying the retinal foci. Edema was severe and dissociation of structure, migration of pigment and extensive venous congestion (vessels contained nucleated red cells) were present; capillary hyperplasia and vascular proliferation were not significant. The retina was for the most part artefactitiously separated but showed areas of subretinal hemorrhage. The granular layers were well developed, and the outer showed few oval nuclei. Cones and rods were partly destroyed in areas and associated with hemorrhage and appeared ill formed (partly due to fixation and processing). The granular layers were not so compact as in the adult state. The ganglion cell layer was poorly represented. The pigment layer of the retina was of a heavy negroid type. Müller's fibers were greatly exaggerated and hyperplastic in the inner layers, which were not fully differentiated and showed new connective tissue. The nerve fiber layer was loose, wide and disarranged. A few plasma cells, lymphocytes and mononuclear cells had infiltrated, and histiocytes, storing pigment and debris, were noted. An occasional cystlike aggregate of toxoplasmas was seen in the inner nuclear layer, and not in the severe destructive granulomatous areas in the retina. One cluster was observed at the level of the nerve fiber layer. Inflammatory foci were mostly retinal and gave the impression that this layer was the point of origin. The macular area was occupied by a large, swollen necrotizing lesion. Plasma cells were noted in moderate abundance, as well as a few lymphocytes. The necrotizing retinal lesion showed disintegrating cells, some of which had been flung into the vitreous—dissociation and migration of pigment were pronounced as one proceeded inward. Hemorrhage was noted on the surface of the retina. No parasites were seen in the necrotizing lesion.

The optic nerve in longitudinal section showed persistence of the hyaloid artery, extending partly into the vitreous. The lamina cribrosa was less compact than in the adult eye and proceeded straight across the scleral opening. Edema bordered the central vessel meniscus, and the nerve head was likewise edematous; no foci were noted in the optic nerve substance. The leptomeninges showed foci of lymphocyte infiltration. A physiologic cup was not present. The vaginal space was open.

In general except in the area centralis the cells and tissue layers of the retina of a 7 month old human fetus are arranged like those of the retina of an adult. This was true in the case presented. The impression was that the inflammatory process was unusually severe, selective and discrete and had not had time for repair. The pigment had not collected in depots, and no fixed scar had evolved. No calcium was noted in the retina or the choroid.

Case 2.—L. H., the identical twin of the preceding patient, was likewise born by frank breech delivery but was in good condition immediately on birth and was the larger of the twins.

On admission to the hospital he weighed 5 pounds and 8 ounces (2,494.8 Gm.). He was somewhat inactive but responded well to external stimuli. There was a mild degree of separation of the cranial sutures. Otherwise the patient appeared to be a normal premature infant. The laboratory data on admission were noncontributory.

Course.—Like his brother, the patient became icteric at the age of 3 days. For two weeks he had a purulent discharge from the umbilicus. He received sulfadiazine by mouth. Although listless, the child ate fairly well. There were episodes of cyanosis and dyspnea. The temperature at times was elevated. Abdominal distention was noted, and the icterus persisted. Nevertheless, the child gained weight and was discharged on September 30, at the age of 25 days.

He returned one week later, October 6, because of diarrhea and symptoms of a cold. From this time on he was under almost continuous observation, either in the ward or in the outpatient department. A thorough investigation was made at the time of his first readmission to the hospital because by this time the autopsy on the twin brother had revealed toxoplasmosis.

Examination.—The following pertinent data were obtained: The child was still jaundiced. The abdomen was distended; the stools were clay colored, and the urine contained bile. The hemoglobin content of the blood was 15 Gm. per hundred cubic centimeters. The white blood cell count was 8,800. The spinal fluid was xanthochromic and contained 500 red cells and 20 white cells per cubic millimeter. The protein content was greatly increased. Neurologic symptoms were absent, and no abnormal physical characteristics were observed in this respect. Roentgenograms of the skull revealed multiple small areas of intracerebral calcification. Later, a mild degree of internal hydrocephalus was demonstrated encephalographically.

The first ophthalmologic examination (Dr. H. L. Begle) revealed uveokeratitis. The corneas were somewhat hazy, and the fundi were at first not clearly visualized. A few days later the fundi appeared diffusely gray. The optic disks were indistinct. Localized lesions were not recognized at this time, owing to cloudy media, nystagmus and difficulty of examination.

Further Course.—The patient remained jaundiced until the fifth month. During most of this time the abdominal distention persisted. The liver and the spleen became palpable for a time. There were several episodes of intercurrent infections accompanied by respiratory symptoms, and on one occasion abscesses developed on both legs. One of these required surgical drainage, and hemolytic streptococci were cultured from the pus. In spite of these setbacks, the patient gained weight and kept pace with the majority of premature infants so far as physical development was concerned. Mentally he appeared slightly retarded when last seen, at the age of 7 months. At this time there was a suggestion of a tonic neck reflex and the right knee jerk was hyperactive. The spinal fluid was examined on several occasions and did not become normal until the patient was 4½ months old.

Through the permission of Dr. Joseph Heidelman, of the Wilmer Ophthalmological Institute, Johns Hopkins Hospital, the serum of each of the patients and of the mother was tested for neutralizing antibodies against the toxoplasma. The method used was essentially that described by Sabin. The serum of the dead twin was obtained at autopsy and was not processed until several days afterward. The results in this case were doubtful. The serums of both the living twin and the mother, which were processed by immediate freezing at —40 F. and desiccated in a vacuum, contained neutralizing antibodies against the toxoplasma.

Ophthalmologic Examination.— Ocular Findings at Eight Weeks (Dr. Begle): The pupils reacted to light; vision was questionable; no fixation on objects was noted; the corneas were still hazy; threadlike extensions of the pupillary borders passed into the upper and the lower quadrant. The disks were sharp now; there were a few circumscribed lesions in the right macular area; the left pupil was undilated.

At 5 months one of us noted that the eyes were smaller than normal and showed irregular nystagmus and dissociation in movement, which was not limited. The left eye usually appeared to converge to about 30 degrees. The cornea of the right eye showed diffuse exudative retinal lesion. A similar, much smaller, lesion was noted in the mesial half of the retina about halfway between the nerve head and the periphery. The borders were round and showed areas resembling hemorrhage; the exudative process and the loss of transparency obscured the retinal vessels.

The left eye showed decided persistence of the fetal vessels around the entire circumference and a smaller, more irregular pupil (in spite of instillation of homatropine drops). It was even more difficult to make out the details in the left fundus, but a similar retinal lesion, resembling exudative chorioretinitis over a limited area, was noted in the temporal half.

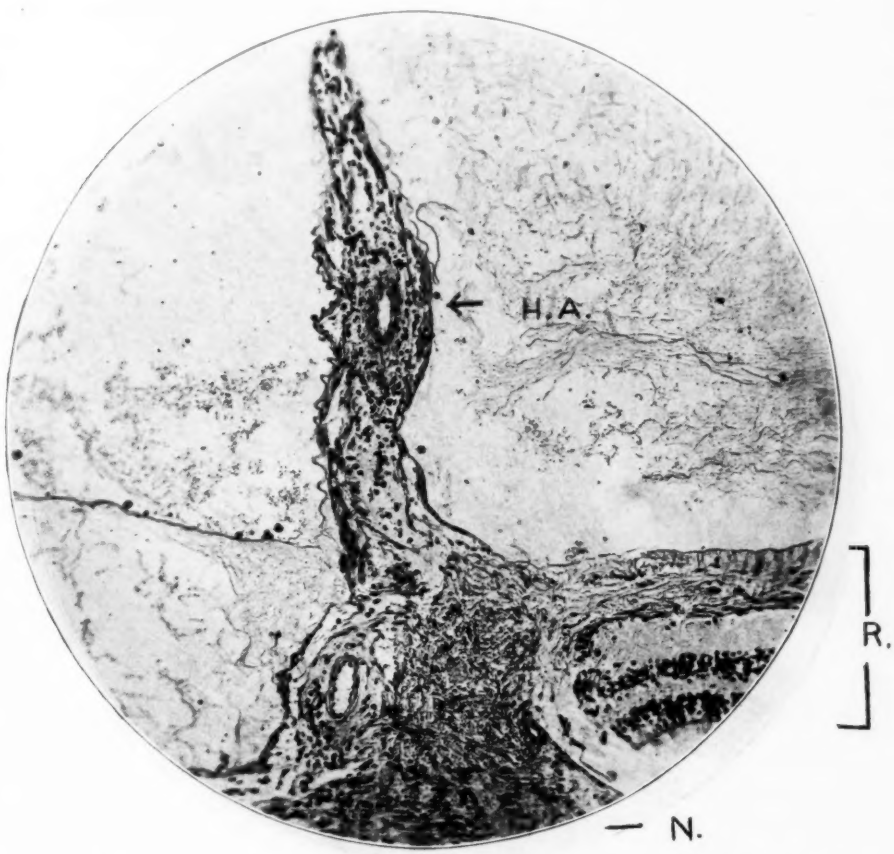

Fig. 4.—Details of the optic nerve head. *H.A.*, hyaloid artery; *R*, retina; *N*, optic nerve.

loss of normal transparency. The anterior chamber was shallow. The pupil reacted to light sluggishly. The patient was attracted toward bright light. The pupil dilated partially and unevenly under the influence of homatropine, owing to partial persistence of the pupillary membrane (especially in the down and in quadrant) and associate posterior synechia. Many vessels originated at the border of the pupil. The media showed some loss of transparency of the cornea, and the lens was apparently clear except where the anterior capsule was disturbed by the pull of the synechia. The vitreous showed diffuse haziness. The optic nerve head appeared congested and somewhat edematous, and the fine details were difficult to see. Central vessels were noted on the nerve head. On the temporal side, including more than the macula and running over to the nerve, was a slightly elevated, whitish to ivory-colored

The use of general anesthesia to permit easier examination was not thought advisable or permitted, but the use of local anesthesia, a speculum and fixation with a lock forceps proved fairly satisfactory. Intraocular pressures were estimated, by digital means, to be low normal.

In general, the impression of these early lesions was as follows: They were severe, large, exudative, elevated and ivory white, with fairly sharp and partly hemorrhagic borders, associated with a good red reflex coming through the adjacent transparent retina and with the vitreous affected only minimally.

Successive examinations of the fundi of the surviving twin have shown that a slow recession of the retinal process is in progress.

The characteristics of the early retinal changes, as illustrated in this case, were multiple bilateral large,

whitish, exudative, elevated macular lesions, which were fairly sharply bordered, sometimes with hemorrhage, and were seen through an only moderately disturbed vitreous.

OCULAR LESIONS IN CONGENITAL TOXOPLASMOSIS

Jankû [13] reported as parasitic cysts (Sporozoa) lesions in the retina of a hydrocephalic infant associated with macular coloboma, and in the left eye with microphthalmos. Levaditi [5] classified Jankû's parasite as the toxoplasma, and also that in a case reported by Torres.

From these reports and our cases, it is evident that this disease in infants is commonly associated with microphthalmos in one or both eyes. The incidence is so high that it is reasonable to assume that the microphthalmos is inflammatory in origin. A small eye may result from uveitis, whether principally anterior or posterior. The persistent vessels seen in the pupillary areas were embryonic and were associated with inflammatory adhesions of the iris to the lens; they represented a fetal vascular persistence plus a fetal iritis. In nearly all of the reported cases

Fig. 5.—Details of the border of the chorioretinal lesion. *R*, retina; *C*, choroid; *S*, sclera.

Vail [8b] and co-workers studied older children and adults and related ocular lesions to positive reactions to neutralizing antibodies against the toxoplasma.

Koch, Wolf, Cowen and Paige [11] reviewed previously reported cases and presented interesting data concerning examinations of the fundus and histologic features of ocular lesions in the posterior segment.

13. Jankû, J.: Pathogenesis and Pathological Anatomy of Coloboma of the Macula Lutea in an Eye of Normal Dimensions and in a Microphthalmic Eye in the Retina, Časop. lék. česk. **62**:1021, 1052, 1081, 1111 and 1138, 1923.

squint, irregular and searching nystagmus, sluggish reaction of the iris to light, pupillary membrane or vessels and low visual acuity were noted.

The chorioretinitis is usually bilateral in toxoplasmosis. It begins in slightly elevated areas, showing in the retina loss of transparency, and soon is converted into an obvious exudative lesion, which is yellowish white, gray or darker red (dependent on age, hemorrhage and pigment) and fairly sharply bordered, with rounded contours. The multiple severe chorioretinal lesions are discrete, and the unaffected areas between, as well as the vitreous, are relatively

clear. This is consistent with the histologic observations, in which the lesions were seen to be rather sharply circumscribed. The size of the involved chorioretinal areas varies from small miliary to large exudative foci. Hemorrhage in the vitreous is not characteristic although opacities of the vitreous were reported in 1 case.

Severe optic neuritis is not the rule. Pigmented borders in the old lesions and over-sclera atrophy are common. The old lesions resemble colobomas and macular dysplasia. The term coloboma may properly include such inflammatory mutilations, although the term is usually applied to noninflammatory lesions.

The age of the lesion in the fundus may be estimated by the presence or absence of blood vessels and their relation to the lesion. According to Mann,[14] the choroiditis of fetal life cannot have begun before the fifth month if the retinal vessels and some layers of the retina are over the patch of destruction. In cases in which the overlying retina is destroyed, together with the vessels in it, which stop abruptly at the edge of the patch, the condition may possibly have arisen during the fifth or sixth month. If the retina becomes involved in a destructive inflammation of the choroid before the disappearance of the vasa hyaloidea propria in the vitreous, it is possible that the lesion may have occurred by or before the third month. A third sporadic type may arise late in fetal life, during the eighth or ninth month, which resembles the choroiditis in the adult and is heavily pigmented.

In our cases, if the inflammation had begun during the first three months of life there would have been a major abnormality or monstrosity of the eye. If the process had been severe before the fifth month the retinal vessels would not have been present, the retina would have been less differentiated and the sclera would have been thinned and bulging or cystic.

In case 1 the patient was an 8 month premature infant and the tissue was studied one month after birth (conception age, 9 months). The anterior and posterior segments showed largely the characteristic development of an eye of a 7 month fetus and partly the development of an 8 month fetus. The macular areas of the retina normally are late in differentiation (after the eighth month). The usual involvement of this part of the retina in infants may be related to the affinity of the parasite for young nerve tissue. No adult ocular lesions have been reported in the acquired form of the disease.[15]

The process in our cases probably originated not later than the seventh month of gestation. The infection apparently retarded, and in some parts of the eye stopped, normal differentiation, as well as produced focal lesions.

While ophthalmoscopic examination may be difficult, owing to the small size of the eyes, the nystagmus and the poorly dilated pupils, the differential diagnosis of early lesions is otherwise relatively easy. The appearance of the bilateral retinal foci and related ocular signs and the general physical findings are usually convincing. The quiescent old lesions require differentiation from healed fetal and acquired chorioretinitis of various causes. Demonstration of neutralizing antibodies against the toxoplasma in the blood of a child and his parents, general physical and psychologic studies and examination of the spinal fluid aid in diagnosis. The extension of such studies to both normal persons and patients with suspicious chorioretinal scars may prove of value. The isolated healed lesions are not pathognomonic.

SUMMARY

Our cases gave opportunity for simultaneous study and description of pathologic lesions and lesions seen with the ophthalmoscope in identical twins. An attempt has been made to date the onset of the lesions on the basis of the developmental stages of the eye and the persistence of fetal structures. In both cases early ocular lesions were demonstrated and are thought to have originated in the seventh fetal month. Our cases demonstrate the destructive affinity of the toxoplasma for young nerve tissue, especially that of the eye.

The conceptional age, the virulence of the parasite and the special susceptibility of tissue may influence the distribution and the severity of the disease.

In the future, other parasites may be found to produce lesions similar to those of toxoplasmosis; hence the importance of a study of the parasite and its properties. The cases reported here offer strong evidence for transplacental infection.

14. Mann, I.: Developmental Abnormalities of the Eye, New York, Cambridge University Press, 1937, p. 181.

15. Pinkerton, H., and Weinmann, D.: Toxoplasma Infection in Mass, Arch. Path. **30**:374-392 (July) 1940. Pinkerton, H., and Henderson, R. G.: Adult Toxoplasmosis: A Previously Unrecognized Disease Entity Simulating the Typhus—Spotted Fever Group, J. A. M. A. **116**:807-814 (March 1) 1941.

FACTORS AFFECTING HEMORRHAGE FOLLOWING EXTRACTIONS OF CATARACTS

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The problem of hemorrhage into the anterior chamber of the eye after the removal of a cataract has always been a disturbing one to ophthalmologists because the hemorrhage prolongs convalescence, it may lead to other complications and occasionally it results in limitation of vision. This problem has been baffling because it has been difficult to ascertain the cause of the hemorrhage.

Many papers dealing with various aspects of the problem have appeared, but three are outstanding among the earlier publications. Between 1869 and 1897 Herman Knapp [1] reported about 2,000 cases. He concluded that trauma accounts for the hemorrhage in a large number of cases but that in many others the cause is unknown.

In 1916 Wheeler [2] reviewed the literature thoroughly and also reported results for a total of 2,123 operations which had been done by various members of the staff of the New York Eye and Ear Infirmary during a ten year period while the type of operation was undergoing a transition from the technic of simple extraction to that of removal of the cataract either with or after iridectomy. He found that hemorrhage occurred least often after preliminary iridectomy and most frequently when the cataract was removed with simultaneous iridectomy. He also noted that a higher percentage of hemorrhages occurred in the 40 to 50 year old patients group and suggested that the greater activity of persons of this age group might be more significant in causing trauma than the dementia and irresponsibility of elderly patients.

Derrick Vail Jr. published a careful study of the problem of hyphemia in 1933 [3] and included the following points among his conclusions:

1. The incidence of hemorrhage, as derived from a review of the literature and as substantiated by his own work, was 7.6 per cent of the total number of operations for removal of cataracts.

2. Sex, age and general health play a minor role, if any, and the cause of hemorrhage is chiefly a local factor.

3. In the vast majority of cases hyphemia is due directly to trauma.

4. A "constitutional moment" exists for the eye between the third and the sixth day, when external pressure is most likely to cause hemorrhage. This "constitutional moment" is related to the rapidity with which the anterior chamber fills, and hemorrhage apparently occurs more readily when a conjunctival flap and sutures give tight closure of the wound to hasten the filling process.

5. Hyphemia occurred less frequently after simple extraction, with which filling of the anterior chamber was less rapid, but prolapse of the iris was a common and serious complication with this operation.

6. Preventive treatment is important, the time of the first dressing being critical and careful nursing for the first seven days essential.

From these studies it is apparent that trauma is an important cause of hemorrhage. The type of operation and its effect on intraocular pressure are responsible for the hyphemia in some cases. Certain unknown factors likewise play a role. In an effort to understand these factors I began an investigation in which each patient was carefully studied. That I might be able better to evaluate the factors which cause hemorrhage, I undertook detailed examinations of the

Candidate's thesis for membership in the American Ophthalmological Society, submitted May 29, 1944.

1. Knapp, H.: Report and Remarks on a Third Hundred of Cataract Extractions, Arch. Ophth. **1**:103, 1869; Report and Remarks on a Fourth and Fifth Hundred of Cataract Extractions According to von Graefe's Method, ibid. **6**:3, 1877; Report and Remarks on a Sixth Hundred of Cataract Extractions Performed According to von Graefe's Method, ibid. **8**:200, 1879; Report of a Seventh Hundred of Cataract Extractions with Historical and Critical Remarks, Particularly on the Peripheral Opening of the Capsule, ibid. **10**:295, 1881; Report of an Eighth Series of One Hundred Consecutive Cataract Extractions with Remarks, ibid. **12**:69, 1883; Report on a Second Series of One Hundred Successive Cataract Extractions Without Iridectomy, ibid. **18**:1, 1889; Report of a Third Series of One Hundred Successive Cataract Extractions Without Iridectomy, ibid. **19**:280, 1890; Jahresb. f. Ophth., 1897, p. 95.

2. Wheeler, J. M.: A Study of Hemorrhage into the Anterior Chamber Subsequent to Operations for Hard Cataract, Tr. Am. Ophth. Soc. **14**:742, 1916.

3. Vail, D. T., Jr.: On Hyphema After Cataract Extraction, Tr. Am. Ophth. Soc. **31**:496, 1933.

blood and the physical status of the patient. While my study was in progress, a few additional reports which are of interest appeared in the literature.

In 1941 Vail reported [4] an additional series of 675 cases to substantiate his theory that trauma is important but that increased intraocular pressure from rapid filling of the anterior chamber predisposes to hemorrhage.

In 1942 Gradle and Sugar [5] published results of an interesting study in which they had attempted to evaluate the forces which might affect the degree of tension in a cataract wound. They measured the increase in intraocular pressure due to the forcible contraction of the orbicularis palpebrarum, the compressibility of the orbital tissues and the degree of protrusion of the eyeball. They concluded that the first of these factors is the most significant, and accordingly they performed a series of 40 operations on private patients using tenotomy of the orbicularis muscle to lessen the chance of increasing intraocular pressure. Their results were 100 per cent successful, and no rupture of the wound or hemorrhage occurred in any patient. In a second series of 52 infirmary patients, however, 9 hemorrhages were noted. This work would appear to substantiate both Vail's theory that external pressure can cause hemorrhage if applied at a critical time and Knapp's and Wheeler's suggestion that unknown factors are significant.

In 1942 DeVoe [6] presented a summary of 453 operations for cataract. He had studied various factors which might have caused hyphemia, and in his report he compared the average values for patients who had had postoperative hemorrhage with those for patients who had not bled. His total incidence of hemorrhage was 20.9 per cent. He stated that age, time of year, systolic and diastolic blood pressure, the presence of diabetes or syphilis and elevated intraocular pressure were not found to be related to postoperative hemorrhage. Also the type of operation, the presence or absence of retrobulbar injection, the type of suturing and the skill of the surgeon were not significant, although the performance of an iridectomy at the time of extraction increased the chance of subsequent hemorrhage by about 20 per cent. DeVoe's determinations of the level of ascorbic acid in the plasma and his tests for capillary fragility gave values which lacked correlation and which were not reliable in predetermining hemorrhage. He concluded that neither vitamin C subnutrition nor a deficiency of prothrombin in the plasma associated with lack of vitamin K is an important cause of hemorrhage following extraction of cataract. Certain systemic measures, such as the use of snake venom, calcium, thromboplastic substances, protein diets and various proprietary drugs, were tried but did not appear useful as preventive agents of hyphemia.

Although DeVoe has made a careful, critical summary of a large number of cases, his gross analysis has failed to reveal the factors which are routinely responsible for hemorrhage. I have approached the problem from a slightly different point of view. Instead of utilizing only average results or statistical analyses, I have attempted to evaluate individual cases. For this purpose I have done complete blood counts and platelet counts, measured the bleeding time and the coagulation time, made clot retraction and tourniquet tests, taken the blood pressure and made determinations of hemoglobin, blood sugar and nonprotein nitrogen, as well as made a complete physical examination of each patient, together with a review of his past tendencies toward bleeding.

A few authors have mentioned similar but less complete studies of the blood, but none has reported results for a carefully controlled series of cases. Turner [7] stated in 1935: "The coagulation and bleeding time should be taken. If these do not conform to good surgical practice, the operation should be postponed until this element can be corrected or the risk minimized." Goar [8] in 1938 advised preliminary administration of calcium if the bleeding or the clotting time is long. Berens and Bogart [9] (1938, 1941) did determinations of coagulation and bleeding time in addition to the usual blood counts and hemoglobin estimations, but these authors have not presented the details of their results. They considered increased intraocular tension an important predisposing factor for hyphemia. Meyer [10] in 1929 measured the platelets, the serum calcium, the bleeding time, the coagulation time, the capillary fragility and the excretion of vitamin C of 8 patients; he found a correlation between deficiency of vita-

4. Vail, D. T., Jr.: Hyphema After Cataract Extraction, Am. J. Ophth. **24**:920, 1941.

5. Gradle, H. S., and Sugar, H. S.: Wound Rupture After Cataract Extraction, Am. J. Ophth. **25**:426, 1942.

6. DeVoe, G.: Hemorrhage After Cataract Extraction: A Clinical and Experimental Investigation of Its Cause and Treatment, Arch. Ophth. **28**:1069 (Dec.) 1942.

7. Turner, H. H.: Preoperative Study of Cataract Patient, Pennsylvania M. J. **38**:840, 1935.

8. Goar, E. L.: Management of Complications of Intraocular Surgery, Am. J. Surg. **42**:62, 1938.

9. Berens, C., and Bogart, D.: Postoperative Complications of Cataract Extraction, Am. J. Surg. **42**:39, 1938; Immediate Complications of Operations for Acquired Cataract, ibid. **54**:346, 1941.

10. Meyer, F. W.: Ueber die postoperative Nachblutung nach Starextraktion und ihre Ursachen, Klin. Monatsbl. f. Augenh. **102**:479, 1929.

min C and of capillary fragility in 7 of them. Taube [11] in 1938 had bleeding at an operation for preliminary iridectomy in a case in which the tourniquet test gave a positive reaction for capillary fragility. The cataract was removed successfully after vitamin C therapy had been given for four weeks. Urbanek and Albrecht [12] (1938) found the incidence of hemorrhage higher in an institutional group whose deficit in vitamin C (measured by tests of excretion) was greater than was found for private patients. Foss [13] (1941) determined the prothrombin time for 54 patients with cataract and concluded that hemorrhage is not due to a deficiency of vitamin K. The reports of these authors give some clues in regard to constitutional conditions which may cause bleeding after operations for cataract. The purpose of my investigation has been to study these factors in more detail so that they may be evaluated in relation to the whole problem of hyphemia.

METHODS

The following technics have been employed in my study of individual patients. Whenever possible, determinations were done in duplicate to insure accuracy of results. Many of the tests were done in the special hematologic laboratory.[14]

1. Red and white blood cells were counted and hemoglobin determinations made on fasting oxalated whole venous blood. The blood was diluted with Hayem's solution for the red cell counts and with 1 per cent acetic acid for the white cell counts. A Neubauer counting chamber was used. Hemoglobin was determined by means of photoelectric colorimetry. In preparing slides for differential counts of leukocytes Wright's stain was used, and 100 cells were counted.

2. The number of blood platelets was determined by direct counts on capillary blood with the aid of an isotonic diluting fluid containing a stain and an anticoagulant, according to the method of Pohle (1939).[15]

3. Bleeding times were determined from a puncture of the lobe of the ear by the method of Duke, the blood being blotted every fifteen seconds on absorbent paper to estimate the rate of decrease and the final cessation of hemorrhage. The normal for this technic has been reported to be from one to three minutes.

4. Coagulation times were measured on venous blood by the method of Lee and White as modified by Pohle and Taylor [16] (1937). Two small test tubes were filled with 2 cc. each of venous blood and kept at 37 C. From time to time the first tube was gently tilted to test for the onset of clotting. The second tube was kept in reserve and tested as coagulation started in the first tube, thus serving as a check on accuracy. Normal values were between six and twelve minutes.

5. Clot retraction times were measured by observing the number of hours before 2 to 3 cc. of clotted blood began to separate from the wall of the test tube with beginning expression of serum.

6. The Rumpel-Leede tourniquet test was used to determine capillary fragility. A pressure midway between systolic and diastolic was maintained for seven and one-half minutes by means of a blood pressure cuff applied just above the elbow. Petechiae were counted in a 1 inch (2.5 cm.) square 2 inches (5 cm.) below the antecubital fossa after the cyanosis had cleared. From 0 to 12 petechiae were considered normal; 12 to 20 were considered an equivocal value, and more than 20 were thought to afford positive indication of capillary fragility.

7. The sugar content and the nonprotein nitrogen content were determined on fasting, oxalated, whole venous blood by the classic Folin and Wu copper reduction method for sugar and a micromodification of the Kjeldahl-Folin technic for nonprotein nitrogen.

The following standards were used in estimating hyphemia:

1. A small amount of blood found in the anterior chamber at the time of the first dressing was considered hemorrhage from the surgical operation.

2. Any amount of blood appearing after the first dressing was considered postoperative bleeding.

3. Degrees of hyphemia were based on the following criteria: 1 degree, 1 mm. or less of blood in the anterior chamber; 2 degrees, ¼ mm. of blood in the anterior chamber; 3 degrees, the anterior chamber full of blood; 4 degrees, the anterior chamber full of blood plus opening of the wound.

RESULTS

In the series which I am reporting there were only 98 patients, but an attempt has been made to make a thorough study of each. Before I discuss the details and the significance of my results, it is interesting to note the conclusion which is reached if averages are studied. My patients with cataract have been divided into two groups according to whether or not they had postoperative hemorrhage. Table 1 presents a summary of the range and the average results of the tests which were used to evaluate the status of each patient. I wish to call attention to the fact that the average values for patients with hemorrhage are not significantly different from the average results for patients who did not have postoperative bleeding. Thus, at first glance my work would seem to confirm the conclusions of those previous authors who have stated that age, systolic and diastolic blood pressure, anemia,

11. Taube, E. L.: Cataract Extraction in Subclinical Scurvy, Am. J. Ophth. **21**:910, 1938.

12. Urbanek, J., and Albrecht, W.: C-Vitamin und Lebensalter, Ztschr. f. Augenh. **95**:129, 1938.

13. Foss, B.: Gibt es eine K-Vitamininsuffizienz bei Blutungen nach intrabulbären Eingriffin? Acta ophth. **19**:15, 1941.

14. Dr. O. O. Meyer has made suggestions and has supervised the hematologic studies for this investigation. Dr. F. J. Pohle has personally performed many of the determinations.

15. Pohle, F. J.: The Blood Platelet Count in Relation to the Menstrual Cycle in Normal Women, Am. J. M. Sc. **197**:40, 1939.

16. Pohle, F. J., and Taylor, F. H. L.: The Coagulation Defect in Hemophilia: The Effect in Hemophilia of Intramuscular Administration of a Globulin Substance Derived from Normal Human Plasma, J. Clin. Investigation **16**:741, 1937.

platelet level, bleeding time, coagulation time, results of tourniquet tests and the existence of diabetes or nephritis are not significant factors for predicting the occurrence of postoperative hemorrhage.

A total of 205 operations were performed on the 98 patients.[17] They have been summarized in table 2 according to the type of operation and the number of hemorrhages. In chart *A* the data are graphically presented, with the results grouped together for each ten year age period. The operations which were followed by hemorrhage have been divided according to whether or not known trauma was responsible for the bleeding.

It is at once apparent that the greatest frequency of hemorrhage took place with the combined intracapsular extractions. In this group of operations the incidence of bleeding was 20.6 per cent, in contrast to 7.8 per cent for intracapsular extractions after preliminary iridectomies. There were only 3.2 per cent of hemorrhages following preliminary iridectomies. The total incidence of hyphemia for the whole series was 11.2 per cent. Trauma was known to be instrumental in 48 per cent of the cases of hemorrhage. These results substantiate the theories of Wheeler and Vail that the type of operation and trauma are two important factors influencing postoperative bleeding.

Since the results thus far summarized do not contribute any new insight into the problem of hyphemia and since the use of averages obscures factors which may be important, I have prepared table 3 to present some pertinent facts about the individual patients of my series. In this table are included the more important laboratory data for all patients who had postoperative hemorrhage. When the data for patients without known trauma are contrasted with the data for patients whose bleeding was precipitated by trauma, the following findings appear worthy of comment:

1. As has been previously noted, the greatest number of hemorrhages occurred with combined intracapsular extractions. Trauma had no special significance in these cases, since 6 of the 13 patients had had no known trauma.

TABLE 1.—*Data on Patients Having Cataract Operations*

		Blood Pressure			Non-protein		Red	White		Bleeding	Coagulation	Tourniquet
	Age	Systolic	Diastolic	Sugar	Nitrogen	Hemoglobin	Blood Cells	Blood Cells	Platelets	Time	Time	Test
77 patients without hemorrhage												
High	80	230	130	132	45	17.6	7.15	15,800	394,000	4	12.5	28*
Low	34	96	50	55	24	11.1	3.6	5,000	145,000	1	3.5	0
Average	65	152.7	87.4	114.9	35.4	14.3	4.6	9,500	273,800	1.6	7.1	2.9
21 patients with postoperative bleeding												
High	83	198	115	110	42	17.6	9.25	12,350	320,000	3	9	18
Low	50	106	70	72	20	6.6	3.93	5,600	175,000	1	3	0
Average	67	148.7	92.1	95.7	33.3	15.2	5.3	8,900	261,600	1.4	6.5	4.6

* Two patients with values of 68 and 49, which were corrected after vitamin C therapy to 17 and 2, were not included in this table.

TABLE 2.—*Summary of Types of Operations and the Number of Hemorrhages for Each*

Type of Operation	No. of Operations	No. of Patients	No. of Hemorrhages
Preliminary iridectomy	62	43*	2
Intracapsular extraction after preliminary iridectomy	51	36	4
Extracapsular extraction after preliminary iridectomy	11	7	0
Combined intracapsular extraction	63	39	13
Combined extracapsular extraction	18	16	4
Totals	205	98	23

* These are not included in the total.

2. The severity of the hemorrhages was comparable for the patients who had undergone trauma and for those who bled without known trauma. Among patients without trauma there were 6 instances of 1 degree hyphemia and 3 instances each of 2 degree and of 3 degree hyphemia. In the traumatic group 4 patients had 1 degree, 5 had 2 degrees and 2 had 3 degrees of hyphemia. There was no occurrence of 4 degree hyphemia.

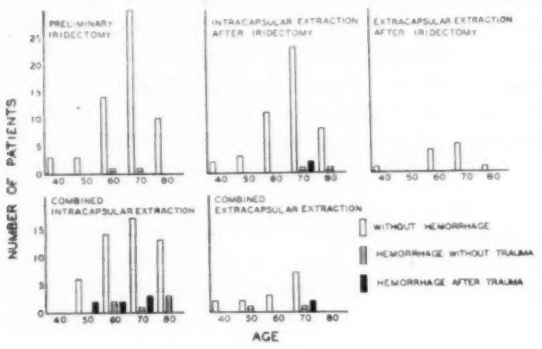
3. Hemorrhages occurred from the third to the twelfth day after preliminary iridectomy. They occurred more often at about five or six days for the series as a whole. This result is in accord with the experience of other workers.

4. The occurrences of hemorrhage were equally divided between men and women for those who bled without trauma, but 80 per cent of those who bled after trauma were men. Perhaps males are more prone to have traumatic episodes.

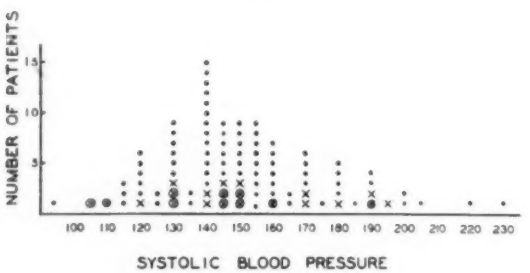
5. Blood pressures for my entire series ranged from 96 systolic and 50 diastolic to 230 systolic and 120 diastolic, varying in the bleeding patients from 106 systolic and 74 diastolic to 198 systolic

17. These operations were executed by both attending doctors and resident staff members at the Wisconsin General Hospital. The technic for the intracapsular extractions and the preoperative and postoperative care of the patients has been discussed in detail by Davis (Personal Experiences with Intracapsular Cataract Extractions, Tr. Am. Acad. Ophth. **42**:235, 1937).

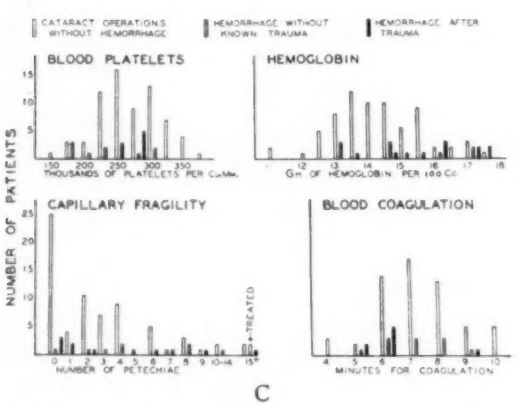
and 108 diastolic. The hemorrhages were about equally distributed throughout the entire range of these blood pressures, but 5 patients without trauma had a systolic pressure higher than 150 with a diastolic pressure of over 100, in contrast to only 1 hypertensive patient among those with trauma. The latter bled after each of two operations. In chart *B* the systolic pressures are



A



B



C

A, distribution of 205 operations for cataract on the basis of type of operation, age and incidence of hemorrhage. *B*, the relation of blood pressure to hemorrhage. Dots represent operations for cataract not followed by hemorrhage; crosses represent postoperative hemorrhage without known trauma; encircled crosses represent hemorrhage following trauma postoperatively. *C*, factors affecting postoperative hemorrhage.

illustrated for all 98 patients. This graphic presentation helps one to visualize the fact that hypertensive patients are more likely to bleed without the added tension produced from trauma. Diastolic pressures have not been charted, but they closely followed the systolic pressures in deviations from the normal.

6. Only 3 patients among those with hemorrhage were markedly overweight or underweight, and all of these were in the group whose bleeding took place after trauma. This may or may not mean that malnutrition when manifest as underweight or as overweight is important in relation to hyphemia. Undoubtedly malnutrition might be significant if it were correlated with those deficiencies in minerals or in vitamins which have a direct relationship to hemorrhagic tendencies.

7. Four patients among those with hyphemia had blood platelet levels of about 200,000 or lower. It seemed pertinent, therefore, to study all patients graphically with respect to platelet levels, and the results are shown in chart *C*. It will be noted that the incidence of hemorrhage was much greater for the lower platelet levels and that nearly one half of all patients with blood platelet levels below 200,000 had postoperative bleeding. Trauma was not required to initiate the bleeding of any patient who had a platelet level below 250,000. Thus the platelet level may be one of the factors which are important for determining whether or not bleeding will take place after an operation for cataract, and trauma is less significant as a factor in causing hemorrhage for patients who have low blood platelet counts.

8. There was more tendency toward bleeding among patients with high levels of hemoglobin than among patients with average levels of hemoglobin in their blood. Chart *C* shows that 6 of the 10 patients with values of 17 to 18 Gm. of hemoglobin had hyphemia and that 4 of the 8 patients with 16 to 17 Gm. of hemoglobin also bled. It also shows that trauma was an additional factor in 2 of the 6 hemorrhages reported at the 17 Gm. hemoglobin level and for 3 of the 4 shown at the 16 Gm. level. Thus it is not known whether the trauma or the high level of hemoglobin had the greater significance in producing the bleeding. Hypertension was an additional factor in 2 patients, and 2 others had low blood platelet values, a fact which indicates that factors other than the hemoglobin level may have been decisive in causing the bleeding. One of the patients who bled repeatedly and severely without trauma, however, was diagnosed as having polycythemia vera. Venesection before a subsequent operation was successful in preventing further hemorrhages in this patient. Only 1 patient was seriously anemic, with a hemo-

globin content of 6.6 Gm. This patient bled after trauma.

9. The data for the tourniquet test of capillary fragility are presented in both table 3 and chart *C*. In the group who had 2 or fewer petechiae in their tests there were 40 patients who did not bleed, in contrast to the 8 who did have hemorrhage. Six of the latter had trauma had the exceptionally high petechial counts of 68 and 49 were given vitamin C therapy before surgical procedure was begun. Operations were successfully performed without the occurrence of hemorrhage after their petechial counts had been reduced to 17 and 2 respectively.

10. The coagulation time did not appear to be an important factor in hyphemia, but less

TABLE 3.—*Data on the 21 Patients Having Postoperative Hemorrhages*

Sequence and Type of Operation *	Hyphemia		Age	Sex	Blood Pressure	Hemoglobin, Gm.	Platelets	Bleeding Time, Min.	Coagulation Time, Min.	Tourniquet Test, Petechiae	Cause of Trauma
	Degree	Day									
CEE	1	5	50	M	150/ 94	14.9	284,000	2	7	8	
PI	—										
OIE	1	6	71	M	144/104	17.0	186,000	1	8	4	Out of bed
IAP	2	6									
CIE	3	6	75	M	120/ 70	14.7	175,000	1	5	5	
CIE	1	7	75	M	130/ 80	14.9	312,000	1.5	6	0	
CIE	1	5	76	M	172/108	17.1	300,000	1	6	7	
CIE	—	..	..	..	.....	17.6					
PI	—										
IAP	1	11	83	M	198/108	13.0	247,000	1	6	6	
CIE	2	4	55	F	125/ 75	17.6	249,000	1	7	8	
CIE	—										
PI	—										
EAP	—										
OIE	2	9	58	F	170/110	15.1	306,000	3	8	4	
PI	3	3	59	F	180/108	17.6	204,000	3	7	3	
IAP	—										
CEE	—										
CEE	1	4	70	F	190/115	16.1	184,000	2.5	9	18	
PI	—										
EAP	—										
PI	3	3	73	F	150/ 90	13.0	283,000	1	8	2	
EAP	—										
CIE	1	5	51	M	190/110	16.1	281,000	1	6	0	Bumped eye
CIE	2	5	51	M	162/108	....	.....	..	..	..	Sneezed
CIE	2	5	59	M	106/ 74	6.6	279,000	1	6	1	Removed dressing
CIE	1	6	61	M	110/ 80	16.4	280,000	1.5	6	2	Struck eye
CIE	2	6	65	M	130/ 70	16.4	250,000	1	9	9	Rolled on to eye
PI	—										
PI	—	..	..	..	.....	....	.....	..	..	..	Bumped eye
IAP	2	5	72	M	134/ 90	13.6	275,000	1	5	0	Removed dressing
IAP	—										
CIE	1	4	72	M	150/110	17.1	283,000	1	6	0	Bumped eye; out of bed
CEE	3	6	73	M	146/ 90	15.8	274,000	1.5	5	1	Struck eye
CEE	1	4	73	M	160/ 88	17.1	320,000	1	3	..	Plucked at bandage
CIE	2	5	66	F	152/ 88	14.9	.....	..	..	..	Startled; sat up
PI	—										
IAP	3	5	72	F	145/ 85	13.4	260,000	1.3	6	10	Disoriented
PI	—	..	..	..	.....	....	.....	..	..	..	Removed dressing
EAP	—										

* Key to abbreviations in this column: PI, preliminary iridectomy; IAP, intracapsular extraction after preliminary iridectomy; EAP, extracapsular extraction after preliminary iridectomy; CIE, combined intracapsular extraction; CEE, combined extracapsular extraction.

as a factor in producing the hemorrhage. The incidence of hemorrhage was much higher among the patients with higher petechial counts. Of the 15 patients with petechial counts of 7 or higher, 6 had postoperative bleeding, but in only 2 of these was trauma an additional factor. Thus, hemorrhage is more common and trauma less significant when the tourniquet test indicates greater capillary fragility. Two patients who trauma was required for bleeding among patients with higher coagulation times.

11. No abnormal values for clot retraction were found for any of the patients of my series, and the bleeding times for all were within the range of one to three minutes.

12. Past histories of the patients in regard to tendencies toward bleeding were unreliable for predicting whether or not hemorrhage would

occur with the extraction of a cataract. Ten of the patients gave past histories of easy bleeding or bruising, but only 2 of these had hyphemia at the time of operation. These 2, however, bled without known trauma.

13. Since trauma was a factor in one half of the cases of hemorrhage, I have included in table 3 the types of accidents that occurred. Five patients bumped or struck their eyes, 1 rolled onto his eye, 4 plucked at or removed their bandages, 2 got out of bed, 1 sneezed violently and 1 was startled and sat up suddenly when a window blew open. It is evident that only the last 2 of these happenings were unavoidable accidents. It is well known that the management of these patients is difficult, but it would seem that if more care were taken in advance to gain their cooperation at least some of these accidents might be avoided.

COMMENT

My data apparently confirm the work of others who have found a higher incidence of hemorrhage after combined intracapsular extractions. I should like to suggest, therefore, that preliminary iridectomies should be done whenever possible. In a state hospital this is frequently impossible, but it is worth considering when time and expense need not be so closely considered.

The details of these data have been presented in the hope that they may be of service in bringing the problem of postoperative hemorrhage closer to solution. I am well aware that this evidence cannot be considered a final answer. It seems, however, that this critical analysis of individual cases brings out significant findings which are concealed or obscured when only average results in a large series are considered. It also seems that the separate analysis of cases with and without known trauma has brought greater insight into the factors which cause bleeding. These data tend to emphasize the importance of the physical status of the patient. In those patients whose bleeding was initiated by trauma the results of the tests were within a more normal range. In those patients who bled without traumatic incidents abnormal values (or values at the upper and lower ranges of what has been considered normal) were commonly found. Most significant among such abnormal values were: hypertensive levels of systolic and diastolic blood pressures, low blood platelet values, both low and high amounts of hemoglobin, capillary fragility as indicated by positive results of tourniquet tests, and increased blood coagulation times. I assume that none of these factors is of absolute importance in causing the bleeding but that the actual hemorrhage occurs when the proper combination of circumstances is present.

SUMMARY

The type of operation and the application of trauma at a critical time are two fundamentally important factors in causing bleeding after surgical intervention for cataract, but the constitutional background of the patient has a definite significance. The tests mentioned in this report cannot be used to predict which patient will have postoperative hemorrhage, but they can point out abnormalities that make bleeding more likely. Whenever possible, grossly abnormal conditions should be corrected before any operation is performed. I should like to reiterate Vail's suggestion as to the importance of preventive treatment and his emphasis on the critical time during the first seven days and on the need for careful nursing.

GLAUCOMA DUE TO PERIPHERAL ANTERIOR SYNECHIAS AFTER OPERATION FOR CATARACT

PETER C. KRONFELD, M.D., AND JOSEPH S. HAAS, M.D.
CHICAGO

The multiple factors which influence the intraocular pressure are so closely interrelated and regulated in the normal human being that it is almost impossible to attribute a given rise in intraocular pressure to the action of any single factor. Even in the case of the best known rise occurring in the normal human eye, that during Valsalva's experiment, one is unable to decide whether the cause is an increased volume of blood in the uvea or an interference with the function of Schlemm's canal. Ocular disease occasionally singles out one of the main factors concerned with the regulation of the intraocular pressure and thus creates a glaucomatous state with a much simpler mechanism than that underlying the normal intraocular pressure. A classic example of such a glaucomatous state is the one caused by peripheral anterior synechias following prolonged absence of the anterior chamber after operation for cataract. It is reasonably certain that in eyes affected in this way normal conditions prevailed before the operation with regard to the balance of the intraocular pressure and that only the outflow of intraocular fluid became disturbed by the formation of peripheral anterior synechias. The detailed study of such eyes promised to yield information of value for the understanding not only of this type of glaucoma but also of problems of regulation of the intraocular pressure in general. It was for these two reasons that the present study was undertaken.

MATERIAL

This study concerns itself with states of persistently elevated intraocular pressure of aphakic eyes in which (1) careful examination before the extraction of the cataract, including at least one tonometric reading, had revealed no sign of glaucoma; (2) the inflammatory postoperative reaction was slight and either had completely subsided or was definitely diminishing in intensity fourteen days after the operation; (3) the anterior chamber had been absent for at least six days after the operation; (4) extensive peripheral synechias were found on gonioscopic examination; (5) the severity of the glaucoma closely paralleled the extent of the peripheral anterior synechias, and (6) observation of the normal mate after the surgical procedure revealed no sign of glaucoma.

All services of the Illinois Eye and Ear Infirmary were combed for cases that met the foregoing requirements. Invariably in the cases found no sutures or only conjunctival sutures had been used during the operation for cataract. Thus it appears highly probable that the absence of the chamber was caused by external fistulation. In several cases it was shown that the synechias preceded the glaucoma and did not change in extent during the continuance of the latter except as the result of operations.

The following phenomena were made the subject of study: (1) the diurnal variations of the intraocular pressure; (2) the response to parasympatholytic mydriatics; (3) the response to the drinking test; (4) the response to the puncture of the anterior chamber; (5) the response to corneal massage with the tonometer of Schiøtz for two minutes with the 15 Gm. weight; (6) the response to pilocarpine.

After admission and acclimation to the hospital most patients showed diurnal variations of a regular pattern. The taking of measurements was restricted to intervals of four hours to reduce the possibility of thereby altering the intraocular pressure. The curve was invariably of the inverted type, with the low value at 2 a. m. and the high point between 10 a. m. and 2 p. m. (chart 1). At 2 a. m. the patients had to be wakened for the tonometric measurement; at 6 a. m. they were all awake, their morning activities having started only a few minutes before. The slope of the rise was greater than that of the fall. In corroboration of previous findings of Raeder [1] and Kronfeld,[2] the morning rise could be prevented by keeping the patients asleep or could be precipitated earlier by mild exercise at 2 a. m. (chart 2*A*).

Read at the Eighteth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., May 29, 1944. Dr. Haas cooperated in the preparation of this paper by invitation.

1. Raeder, J. G.: Klin. Monatsbl. f. Augenh. **74:** 424, 1925.
2. Kronfeld, P. C.: Am. J. Ophth. **16:**881, 1933.

In 1 case with extreme daily fluctuations the depth of the anterior chamber was measured at the time of the high and of the low pressure by two independent observers. In or near the visual axis the apparent depth of the chamber was slightly but definitely greater at the time of the high pressure (2.47 against 2.12 mm.).

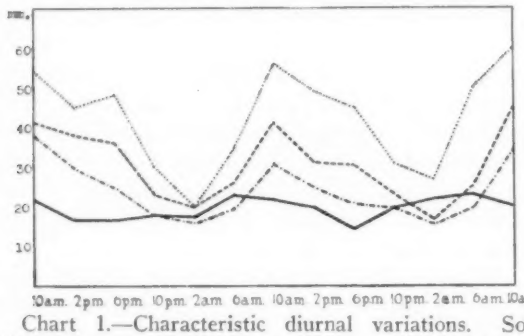


Chart 1.—Characteristic diurnal variations. Solid line represents measurements for normal subject; dots and dashes, those for patient 1; dashes, those for patient 2; dotted line, those for patient 3.

relatively high and could be raised but slightly by glycerin.

Of the parasympatholytic mydriatics, homatropine hydrobromide in 2 per cent concentration was used in the form of instillations at three consecutive tonometric examinations. When given at 10 a. m., 2 p. m. and 6 p. m. it had a definite pressor, or drop-retarding, effect (chart 2 *B*). When it was given at 6 p. m., 10 p. m. and 2 a. m., that is, toward the end of the decline of the intraocular pressure, there was hardly any immediate or late effect. The gonioscopic appearance of the peripheral anterior synechias was not appreciably altered by the instillation of the homatropine hydrobromide.

The drinking tests were done in the morning toward the end of the upgrade or in the early afternoon at the beginning of the downgrade. The result was strikingly positive in all cases, a sharp rise being superimposed on the rising or the falling curve (table 1 and chart 3 *A*).

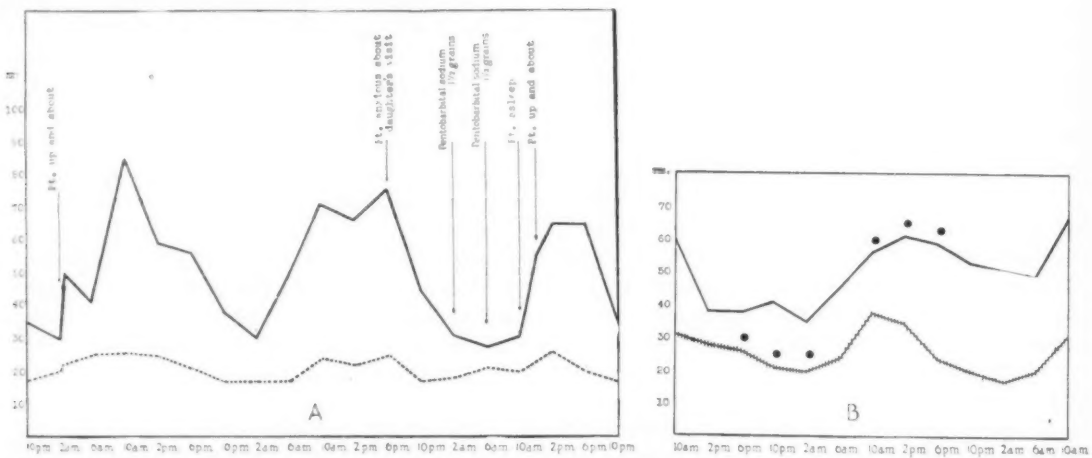

mm.
Ft. up and about
Ft. asleep
Pentobarbital sodium 1½ grains
Pentobarbital sodium ½ grains
Ft. asleep
Ft. up and about
A
B
10pm 2am 6am 10am 2pm 6pm 10pm 2am 6am 10am 2pm 6pm 10pm 2am 6am 10am 2pm 6pm 10pm
10am 2pm 6pm 10pm 2am 6am 10am 2pm 6pm 10pm 2am 6am 10am

Chart 2.—*A*, relation between sleep and intraocular pressure (patient 3). Solid line represents measurements for glaucomatous eye; dashes, for normal eye. *B*, response to homatropine bromide. Crosses represent measurements for patient 1; solid line, those for patient 5; dots, those after administration of 1 drop of homatropine bromide.

In several cases determination of the ocular rigidity after the method of J. Friedenwald [3] was attempted at the time of the turning points. While we are convinced that the Schiøtz tonometer of today is not an adequate or satisfactory instrument for determining rigidity, there was consistency in our findings. The ocular rigidity of patients with small excursions was found not to vary with the intraocular pressure. The rigidity of the patient with extreme fluctuations previously mentioned was lower during the high phase but could repeatedly be raised by instillation of glycerin, which caused disappearance of all visible corneal edema. During the low phase without visible corneal edema the rigidity was

3. Friedenwald, J. S.: Am. J. Ophth. **20**:985, 1937.

TABLE 1.—*Drinking Test*

		Glaucomas					
	Controls	1	2	3	4	5	6
Intraocular pressure before.....	Average 20	26	45	65	35	26	35
Intraocular pressure after *.....	Average 25	40	60	110	56	49	50

* Highest reading obtained during the 60 minutes following ingestion of 1,000 cc. of water.

The response to the puncture of the anterior chamber was a characteristic one in eyes with mild or moderate elevation of the intraocular pressure. The initial drop reached immeasurably low values. The restoration time, that is, the interval necessary for the intraocular pressure to return to the original level, was about as long as or slightly longer than in nonglauco-

matous eyes with chambers having the same volume. The hypertensive phase was absent or slight, both absolutely and as compared with hypertensive phases observed in wide angle glaucomas of the same initial intraocular pressure. The hypotensive phase was also slight or unnoticeable. During the two hours after the puncture of the anterior chamber the nonglaucomatous mate showed a corresponding slight rise of the intraocular pressure.

In 1 patient with marked elevation of the intraocular pressure, two punctures of the anterior chamber were made, at an interval of thirteen days. At the time of the first puncture (7 p. m.) the initial pressure was 53 and was restored in ninety minutes. At the time of the second puncture (7 a. m.) the initial pressure was 53 and was restored in sixty minutes. The same amount of fluid, namely, 0.25 cc., was withdrawn at each puncture. The restoration of pressure in absolute terms was faster in the morning than in the afternoon (table 2).

they would probably show a greater drop during the massage test than nonglaucomatous eyes with initial pressures of from 25 to 33. In the light of this consideration the drop observed in our cases of glaucoma appears very small (table 3). This would tend to substantiate the

TABLE 3.—*Massage Test*

	Controls	Glaucomas								
		1	2	3	4	5	6	7	8	9
Intraocular pressure before massage....	32-29.....	32	38	65	38	45	32	32	28	52
Intraocular pressure after massage....	Average 18 (drop never less than 10)	28	32	61	32	39	28	24	22	45

belief that the massage test is partially indicative of whether the trabeculae and the canal of Schlemm are functioning normally.[5]

Pilocarpine nitrate was effective during the ascent as well as during the descent. It inhibited

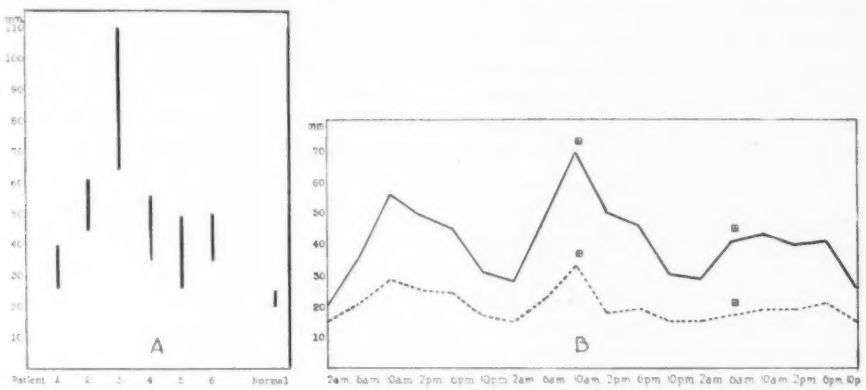


Chart 3.—*A*, results of drinking test. *B*, response to a 2 per cent solution of pilocarpine nitrate. Solid line represents measurements for patient 3; dashes, those for patient 6; crosses in squares, those after administration of 1 drop of pilocarpine nitrate.

TABLE 2.—*Restoration of Intraocular Pressure After Puncture of the Anterior Chamber*

Time	7:00	7:30	8:00	8:30
P. M.	53 (ACP)	4	38	53
A. M.	53 (ACP)	23	53	..

The immediate drop in intraocular pressure due to corneal massage was characteristically slight in all cases. For normal, nonglaucomatous eyes Boeck, Kronfeld and Stough [4] had shown a dependence of the drop on the initial level of pressure, the drop being greater in eyes with higher initial pressure. If nonglaucomatous eyes existed with initial pressure of from 32 to 40

4. Boeck, J.; Kronfeld, P. C., and Stough, J. T.: Effect on Intra-Ocular Tension of Corneal Massage with Tonometer of Schiötz, Arch. Ophth. **11**:797 (May) 1934.

the former and made the latter more precipitous. A single dose of 2 per cent pilocarpine nitrate solution given at 6 a. m. in all cases of mild elvation of pressure prevented a further rise almost completely (chart 3 *B*). Without further medication the next rise in pressure took place the following morning.

COMMENT

The data reported in the foregoing section have a bearing on the diagnosis and the treatment of this form of glaucoma. Tonometric measurements made at or around noon are most likely to reveal the highest pressure reached by the individual patient. Of the provocative tests, introduction of a mydriatic and puncture of the

5. Kukan, F.: Klin. Monatsbl. f. Augenh. **100**:68, 1938.

anterior chamber are not likely to give definitely abnormal results. The massage test and especially the drinking test are more likely to reveal an insufficiency of the apparatus regulating the intraocular pressure.

With regard to conservative therapy, it would seem reasonable to use the miotics during the early morning to prevent the usual morning ascent of intraocular pressure. The first application should be made "the very first thing in the morning," and this should be followed by one to three additional applications during the course of the morning if necessary. During the afternoon and during the night these eyes more or less take care of themselves. An application before the patient retires would be wasted, since its effect would not last until the next morning.

With regard to the possible mechanism of these glaucomas, we are well aware of the dangers of overly simplified concepts. In a system with impaired though probably still adjustable outflow a rapid rise in intraocular pressure from normal or high normal to definitely pathologic levels of pressure might be due to (1) extraocular conditions like lack of the massage action of the extrinsic muscles and the orbicularis; (2) an increase in the volume of blood in the uvea at a rate exceeding the capacity of the channels of outflow; (3) the production of intraocular fluid at a rate exceeding the capacity of the channels of outflow.

Factor 1 could not account for the elevation of the intraocular pressure, since the latter corresponded to periods of increased activity on the part of the patient. Several of our observations would seem to make factor 2 improbable. At the time of the high point of the diurnal variations in pressure the anterior chamber is deeper than at the time of the low. This permits the interpretation that at the time of the high pressure the eye contains more aqueous than at the time of the low. During the ascent the aqueous is regenerated more rapidly than during the low. No hyperemia of the ciliary body or of the iris was noted during the ascent. Determinations of the ocular rigidity did not indicate hyperemia of the posterior segment. We believe the evidence presented suggests that normal production of intraocular fluid exceeds the capacity of the channels of outflow and is the mechanism underlying the morning rises of intraocular pressure observed here. About noon this production stops or becomes reduced to a rate not exceeding the capacity of the outflow channels, whereby the latter are given an opportunity to catch up.

904 West Adams Street.

RETROLENTAL FIBROPLASIA IN PREMATURE INFANTS

V. FURTHER STUDIES ON FIBROPLASTIC OVERGROWTH OF PERSISTENT TUNICA VASCULOSA LENTIS

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Since the last reports [1] on retrolental fibroplasia, sufficient further data have been collected to warrant another communication.

At the time of writing the number of cases registered in this study is 105. In Chicago 20 more have been observed by Dr. E. V. L. Brown and Dr. Justin Donegan and an additional 20 by Dr. Sanford Gifford.[2] Dr. Milton Little,[3] of Hartford, Conn., has at least 15 infants with retrolental fibroplasia under his care. Dr. Stewart Clifford,[3] of the pediatrics staff of the Boston Lying-In Hospital, found that the disease occurs in 12 per cent of infants weighing 1,307 Gm. (3 pounds) or less at birth, but since this percentage is based on less than 50 patients it is not necessarily representative.

In the cases in this study it has been observed that when no complications arise the opaque tissue making up the retrolental fibroplasia usually becomes less dense, so that in places a red reflex can be obtained and in some instances the fundus can be observed in detail. Although this improvement may represent resolution and liquefaction of this opaque tissue, it is more reasonable to presume that the embryonic connective tissue contracts as it matures. As it contracts, its anteroposterior thickness is reduced and may tend to shred, giving rise to spaces, or meshes, through which one can see the details of the fundus. It is obvious that when this occurs the opaque tissue does not form a thin membrane behind the crystalline lens only but tends to invade the entire vitreous humor. The edges of the opaque tissue may appear sharp, but usually when viewed with a slit lamp the fibrillae are gradually reduced in number and density and finally disappear, like the edge of a fleecy cloud. Of course, the apparent reduction in the amount of opaque tissue, which is usual, could result from growth of the eye without growth of the fibroplastic tissue, but this seems unlikely, since eyes affected with retrolental fibroplasia usually grow slowly, if at all. The apparent resolution rarely develops sufficiently to permit good vision. A posterior cortical cataract may develop, however, and increase the opacity, so that the blood vessels in the fibroplastic tissue become obscured. In some instances there is dramatic clearing of the opaque tissue in the vitreous humor, and it is evident that a considerable amount of vision is present. This improvement is most obvious in eyes which have grown appreciably and have anterior chambers of nearly normal depth. When a bright red reflex can be seen and the details of the fundus made out, retinoscopic examination is performed. The eyes of 2 infants were found to be extremely hypermetropic; those of 1 were myopic. In 2 instances glasses were prescribed; these the children tolerated well.

With favorable development, the searching nystagmus, so typical early in the disease, tends to abate and even disappear, and internal strabismus develops frequently. In most of the patients the improvement has been only moderate. Although it is apparent that infants with this condition are conscious of light stimulation and that some of them see relatively large objects which present a great contrast, there is no evidence of ability to judge distance, because these infants never reach for the objects, as do seeing infants of the same age. In an attempt to determine whether or not the fovea had developed and was functioning even moderately well, the parents were asked to use two or three different colored lights, each having a specific meaning—indicating feeding time, bath time and rest time—and to vary the schedule sufficiently so that the color of the light would

Read at the Eightieth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., May 31, 1944.

1. Terry, T. L.: Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis in Premature Infants: (*a*) I. Preliminary Report, Am. J. Ophth. **25**:203 (Feb.) 1942; (*b*) II. Report of Cases, Arch. Ophth. **29**:36-53 (Jan.) 1943; (*c*) III. Embryological Studies, Am. J. Ophth. **25**:1409-1423 (Dec.) 1942; (*d*) IV. Etiologic Factors, Arch. Ophth. **29**:54-68 (Jan.) 1943.

2. Terry, T. L.: Ocular Maldevelopment in Extremely Premature Infants: Retrolental Fibroplasia, Bull. Hist. Med., March 1944.

3. Personal communication to the author.

eventually establish a conditioned reflex. This failed, but the failure may have been a matter of improper establishment of the conditioned reflex rather than an indication that perception of color was entirely lacking. If it were possible to show that discrimination of color is present, the prognosis would be better.

All Caucasian infants born prematurely and observed soon after birth in this study have had a gray-blue iris. For this typical color I have used the term "fetal blue." In cases in which the eyes grow rapidly and the depth of the anterior chambers becomes relatively normal, this fetal blue color is quickly lost, but even in the most severely involved eyes, which grow little or none, there is eventually a definite, but incomplete, change of color. In brunet infants the iris becomes an abnormally dull brown.

As only 3 of the patients showed mental abnormalities at this early date, there seems to be no correlation between retrolental fibroplasia and retardation in mental development of premature infants. Mental retardation does occur in about 10 per cent of all premature infants.[4]

Of the cases originally reported,[1b] case 7 must be disregarded. Pathologic examination of the left eye gave evidence that an unyielding tissue had pulled the retina and optic nerve toward the crystalline lens, thus indicating the method by which retinal folds and retinal separations originate in retrolental fibroplasia. Although this may still be a true concept of how retinal separation develops in many of the infants with typical fibroplasia, the reason for removing this case from consideration is that a younger sister of the patient in this case, born at full term, had the same type of ocular disease as observed clinically in case 7. This must, then, represent a hereditary defect of the eye. The prematurity of the older child was the factor which led to the original inclusion of her case in this study.

In the cases in this series the eyes of the infants which were treated with roentgen rays showed no benefit. Dr. Pelham Glover,[3] of Altoona, Pa., had 2 patients whose eyes he felt improved after implantation of radon seeds. A repetition of his treatment was given in 2 cases in this series; in both instances the eyes not only showed no improvement but exhibited typical phthisis bulbi.

It has already been pointed out that at birth all extremely premature infants have a functioning tunica vasculosa lentis. The venous drainage for this vascular system is through the pupillary portion of the tunica vasculosa lentis, the so-called pupillary membrane, to the anterior surface of the iris. In all infants, including those in whom retrolental fibroplasia later developed, the pupillary portion of the tunica vasculosa lentis, as seen grossly, undergoes involution. It is possible, however, for small vessels of about the size of a capillary to persist at the extreme edge of the pupillary margin of the iris, thus furnishing an invisible drainage for the still functioning tunica vasculosa lentis. It is possible, and even probable, that in some cases the tunica vasculosa lentis behind the pupillary membrane persists without any venous drainage, just as at times the hyaloid artery persists, ending blindly near the lens. As embryonic connective tissue can develop in the meshwork of the tunica vasculosa lentis behind the crystalline lens, so also connective tissue elements may develop around these blood vessels. This new tissue would be inflexible and unyielding and bind the pupil down at these points, and this would give rise to posterior synechia. Before the appearance of the fibroplastic overgrowth, however, the blood vessels circling the pupillary margin were delicate and elastic enough to permit normal dilation and contraction of the pupil. Posterior synechia does develop frequently in infants with retrolental fibroplasia without any evidence of an inflammatory process. Development of fibroplastic tissue around these blood vessels would account, in part at least, for the persistence of the fetal blue or the dull brown color of the irides.

Development of glaucoma is common enough to warrant careful attention; 5 cases have been observed. This does not necessarily mean that the eyes in these cases produce aqueous humor in sufficient amounts to induce this complication. Lack of development of the meshwork of the iris angle and Schlemm's canal would induce glaucoma even where there is an extremely small production of aqueous humor. In these 5 cases the eyes remained microphthalmic. In only 1 instance, a case which Dr. Georgiana Theobald brought to my attention, was hydrophthalmos present. A 1 per cent solution of pilocarpine nitrate was used daily in these cases in an attempt to prevent the development of glaucoma, and no new cases have occurred. Examination of the few pathologic specimens of retrolental fibroplasia showed a poorly developed meshwork of the iris angle. It seems reasonable to presume that hydrophthalmos would invariably arise in these cases if aqueous humor were elaborated in sufficient amounts.

It has already been pointed out that there is a strong tendency toward the development of

4. Rosenoff and Inman-Kane, cited by Hess, J.; Mohr, G. J., and Bartelme, P. F.: The Physical and Mental Growth of Prematurely Born Children, Chicago, University of Chicago Press, 1934, p. 151.

posterior synechia. In an attempt to prevent this, a mydriatic [5] which is effective for only a few hours was used once each week. This prophylactic measure has been less successful in preventing posterior synechia than that used to prevent glaucoma. The effectiveness of these treatments can be determined only through further study. The infants soon resist the use of all collyria as energetically as they can, and such medication is to be avoided when it is really safe to do so. Nevertheless, I have not felt justified in giving it up until either the failure of prophylaxis has been proved or the eyes have shown definite evidence of growth and a deepening of the anterior chamber.

Continued clinical study of this disease has shown that one of the physical findings was incorrectly interpreted. The toothlike processes at the periphery of the opaque tissue were originally called "dentate processes" or "gothic arches." These were thought to represent a serration at the edge, resulting from the insertion of the opaque tissue in the ciliary processes. It was noted that these arches, presumed to correspond to the ciliary valleys, were usually red, like the normal fundus reflex. Sometimes they were dark brown, a color not feasible on the basis of the original interpretation. In 1 recent case, observed when the infant was under ether anesthesia and with the pupil fully dilated, a transilluminator was applied to the sclera for the purpose of determining whether or not a massive intraocular hemorrhage had occurred—a complication that has arisen in some cases. The eye transilluminated well, and from one side a clear view was obtained of this region of "dentate processes." It was obvious at a glance that these red or dark brown areas were in reality the ciliary processes themselves, with the opaque connective tissue of the fibroplasia extending behind them. A study of the ciliary processes under these conditions showed that there was considerable variation in the amount of pigment in this organ. In some cases the processes were red at their extremities, but nearer their bases there was a gradual change to dark red and then to the dark brown of the normally pigmented processes.

The eyes of 2 patients who did not have fibroplasia were examined while they were under ether anesthesia. One had unilateral microphthalmos and the other retinoblastoma. It was possible to see the ciliary processes through dilated pupils, even though the anterior chambers were of normal depth (figs. 1 and 2 *A*). In spite of blue irides, the processes were dark brown and fully twice as wide as those in infants with fibroplasia. In an infant of 4½ months with retrolental fibroplasia, which was absent in one quadrant, the ciliary processes were longer and narrower in the region where the fibroplasia

Fig. 1.—Adult human ciliary processes as seen in an "end piece" removed when the globe was opened for microscopic sectioning. A portion of the cornea which has been cut through obliquely is seen. Note the relation of width of the ciliary processes to that of the ciliary valleys. The black line indicates the extent to which the tips of the processes can be seen through the dilated pupil in a newborn infant's eye.

was most noted (fig. 2 *B*). The ciliary processes were wider and shorter in the quadrant where fibroplasia was lacking (fig. 2 *A*). The ratio of the width of the ciliary processes to the width of the intervening ciliary valleys was 1 : 3 in the region of fibroplasia and 1 : 1.5 in the quadrant

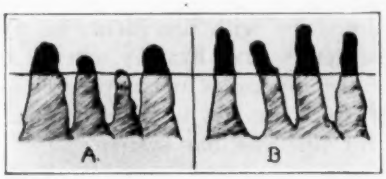

Fig. 2.—Diagram showing variations in thickness and length of ciliary processes in (*A*) a normal infant eye and (*B*) an infant eye containing fibroplasia. The solid black tips represent the part visible in clinical examination with the ophthalmoscope or by means of transillumination. The appearance of the processes in *A* is consistent with the appearance of normal ciliary processes, as shown in figure 1.

where fibroplasia was lacking. If the wider, shorter processes represent the true appearance of normal ciliary processes, then those seen in fibroplasia, often appearing red or free of pigment, are indeed definitely undeveloped—strong evidence that the ciliary body is maldeveloped. A further study of ciliary processes at various times as the infants grow may prove of value in showing variation in rate of development, in pigmentation and in size.

	Gm.
5. Homatropine hydrobromide	0.15
Epinephrine bitartrate	0.30
Cocaine hydrochloride	0.075
Paredrine hydrobromide* 1 per cent..	15.000

*Parahydroxy-α-methylphenylethylamine hydrobromide.

The original concept, that the disease arose through hypertrophy of the intraocular vascular system because of a precociously high blood pressure resulting from premature birth, seems less tenable as the factors are examined more minutely. Thoma [6] pointed out that the effect of increased blood pressure is to keep a vascular system open as well as to cause it to hypertrophy. This is indeed the case in instances of abnormal arteriovenous communication, in which the arteries, relieved of considerable pressure because of the fistula, atrophy and become vein-like, whereas the veins, now subjected to a pressure almost arterial in amount, hypertrophy and become artery-like. In addition, there is an actual increase not only in the width of the capillaries but in the number of capillaries in this bed.[7] At no stage in normal development is the future need for blood vessels anticipated. The blood vessels, considered to be the most adaptable tissue in the embryo and fetus, are not developed at any stage of embryonic and fetal life beyond the needs of the organism at that time. Thus, the blood vascular system is constantly meeting the demand for oxygenated blood from the ever changing tissue as growth and development proceed. High blood pressure itself does not cause widespread new capillary growth, as might be expected from Thoma's [6] hypothesis. The cornea becomes vascularized not because people have high blood pressure but because there is a local need for blood in response to an inflammatory process or an injury. If this reasoning can be used in relation to retrolental fibroplasia with persistence of the tunica vasculosa lentis and hyaloid artery, then the cause of the disease is not a precociously high blood pressure but lies in the fact that there is a need for this vascular system.

Of course, until the cause of this disease process is definitely known, all possible etiologic factors must be considered. In experimental work, attempts were made either to produce the disease or to cause a precocious involution of the hyaloid artery and the tunica vasculosa system in hundreds of opossums and young rats. Although the disease was not produced, repeated dilation of the pupil and examination of the eyes of these animals with an ophthalmoscope did tend to delay the time at which this vascular system disappeared. In the earlier study it seemed highly improbable that precocious exposure to light was an etiologic factor, especially in its effect on the retina per se, despite observation that the process of myelination of the optic nerve appeared to be accelerated in prematurely born infants.[8] Consideration of the possible effect of pupillary response and even of accommodation in premature infants leads to a more plausible cause of the development of fibroplasia. The pupil does contract and dilate in an extremely premature infant in response to exposure to light and to use of a mydriatic, but the possibility of accommodative or other activity of the ciliary muscle is only theoretic.

It is probable that active pupillary responses could embarrass the venous drainage of the tunica vasculosa lentis by stretching and tending to kink the vessels as they extend from the posterior surface around the pupillary margin to the anterior surface of the iris. Should this cause closure of the vessels at the pupillary margin, then perhaps the hyaloid artery and the tunica vasculosa lentis would persist, with considerable passive congestion in them. Passive congestion in itself is not presumed to cause fibrosis, but the edema associated with it can produce fibrosis such as is seen in so-called pulmonary osteoarthropathy.[9]

Again, the pupillary response without, or more likely with, some muscular activity of the ciliary body may tend to open the meshwork of the iris angle. From the appearance of the ciliary body in the fetal eyes one can conclude that aqueous humor is formed before Schlemm's canal and the meshwork of the iris angle is developed sufficiently to take away any or all of this fluid and that this thus produces a higher intraocular pressure—a temporary physiologic "glaucoma." In fact, the mechanism by which congenital glaucoma develops may for a while be active in all eyes as a normal process, being relieved by the development of an adequate device for drainage of aqueous humor from the eye, a development which fails to occur in hydrophthalmos. If the meshwork of the iris angle is opened in a form capable of physiologic activity through the pull of the uveal tract musculature on the scleral spur, then precocious exposure of the eye to light and optic imagery in a prematurely born infant would open the angle and drain aqueous

6. Thoma, cited by Keibel, F., and Mall, F. D.: Manual of Embryology, Philadelphia, J. B. Lippincott Company, 1912, vol. 2, p. 421.

7. Reid, J. R.: Studies on Abnormal Arteriovenous Communications: Acquired and Congenital; Report of Series of Cases, Arch. Surg. **10**:601 (March) 1925; Origin and Nature of Arteriovenous Aneurysms, ibid. **10**:996 (May) 1925; Effects of Abnormal Arteriovenous Communication, ibid. **11**:25 (July) 1925; Treatment of Abnormal Arteriovenous Communication, ibid. **11**:237 (Aug.) 1925; Am. J. Surg. **14**:14, 1931.

8. Salzman, M.: The Anatomy of the Human Eye, translated by E. V. L. Brown, Chicago, University of Chicago Press, 1912, p. 208.

9. Wolbach, S. B.: Personal communication to the author.

humor from the eye, thereby circumventing the occurrence of transitory physiologic glaucoma. This lack of aqueous humor would result in an extremely shallow anterior chamber and a decrease in intraocular pressure, which would fail to stimulate growth of the eye, thus giving rise to microphthalmos. The crystalline lens and the cornea in part obtain their nutrition from the aqueous humor. If nutrition is inadequate, formation of cataracts and corneal opacities, which later occur in retrolental fibroplasia, is explained. Until this aqueous humor is developed in the fetal eye these organs are nourished by the tunica vasculosa lentis system. If aqueous does not develop, then the need for nourishment of the lens and cornea could be supplied by persistence of the hyaloid artery and tunica vasculosa lentis. Thus, lack of accumulation of aqueous humor explains many but not all of the findings in retrolental fibroplasia; the occasional occurrence of glaucoma as a complication needs some further explanation.

Another view is that the ciliary body fails to elaborate aqueous humor. Whether the absence of formation of aqueous humor is the result of lack of permeability of the capillary walls and the ciliary epithelial layers separating the capillaries from the posterior chamber or of lack of an adequate vascular supply to the ciliary processes is purely conjectural. A microscopic study of the few specimens of fibroplasia available showed abnormal ciliary processes in the disease. These were distorted and stretched out but not connected to the fibroplastic mass in every case. Thus, morphologic evidence of abnormality of the ciliary body does exist.

If the ciliary body is at fault because of improper vascular development, it is probable that a more adequate vascular connection could be produced surgically. In considering these possibilities one recalls the proposal made by Sondermann [10] regarding a certain type of glaucoma. He stated the belief that glaucoma could arise from overproduction of aqueous humor in relation to increasing stricture of the vortex vein at the region of the ampulla and substantiated this theory with pathologic specimens. Sondermann said that such glaucoma could be detected by observing fluorescein sodium in the anterior chamber in an extremely short time after an intravenous injection, as compared with the time for a normal eye. He expressed the opinion that there is occasionally a "secretory" glaucoma. He attempted to establish new vascular drainage of the ciliary body by performing a trephination of the sclera over the ciliary body, so that the scar tissue repair of this lesion and the newly formed blood vessels along this tract could connect the circulation of the ciliary body with that of the episclera. In Sondermann's hands this operation has been effective. Provided a better arterial blood supply or a better venous drainage of the cilitary body is needed and can be surgically established, it is possible that this type of operation could be of value in retrolental fibroplasia.

After careful consideration of possible complications, this operation was tried on 1 infant who had unilaterally a marked persistence of functioning pupillary membrane, a shallow anterior chamber, a fetal blue iris and an opacity deep in or behind the crystalline lens. Three weeks after the operation the blood vessels in the pupillary membrane had ceased functioning, the color of the iris improved, the anterior chamber deepened and the eye was growing—a dramatic result. Similar operations have been performed on 18 infants. In 2 the eyes showed so much improvement that each mother requested that the operation be done on the other eye also. Six other eyes have shown improvement after this operation. In 1 patient glaucoma was relieved and did not recur. If the operation is really responsible for the improvement, it is possible that the benefit may be derived from some factor in the operation not now obvious. This operation may have possible therapeutic value for these infants, but this statement is made with hesitation, since the operation has yet to prove its value. In this series, however, no complications have arisen. It should by no means be performed routinely on all infants with retrolental fibroplasia until it has proved its worth in carefully selected cases, in which there is little chance of harm and great chance of improvement. This method of determining the effectiveness of surgical treatment must necessarily be slow, especially when it is considered that many of the eyes operated on show considerable deterioration and would not improve even after an operation of proved value.

The justifiable indications for an operation on such an insecure basis have been in infants with one eye severely involved and the other eye showing little or no involvement or in infants with severe bilateral fibroplasia in whom a complication such as glaucoma, formation of posterior synechia, or development of corneal opacities or a combination of these is beginning to appear.

The technic of the operation is as follows: The conjunctival flap is turned down toward

10. Sondermann, R.: Meine Glaukomtheorie und die Klinik des Glaukoms, Klin. Monatsbl. f. Augenh. **92**: 313-335, 1934; A New Operation for Glaucoma, Ber. u. d. Versamml. d. deutsch. ophth. Gesellsch. **50**:78-81, 1934.

the limbus from about 4 mm. behind. Care is taken to cleanse the sclera thoroughly; a 1 mm. trephine is applied approximately 2 mm. from the limbus. In eyes in which there is practically no anterior chamber, the danger of entering the iris angle is small. In no operation has this happened. A reduction in resistance is usually noted when the sclera has been completely penetrated, but inspection from time to time is the safest guide to knowing when one is approaching the ciliary body. The button is easily removed by gentle dissection, and the flap is replaced. The wound is reclosed with a continuous suture, the lower end of which is left relatively long, so that it can be easily removed without giving another anesthetic. No dressing

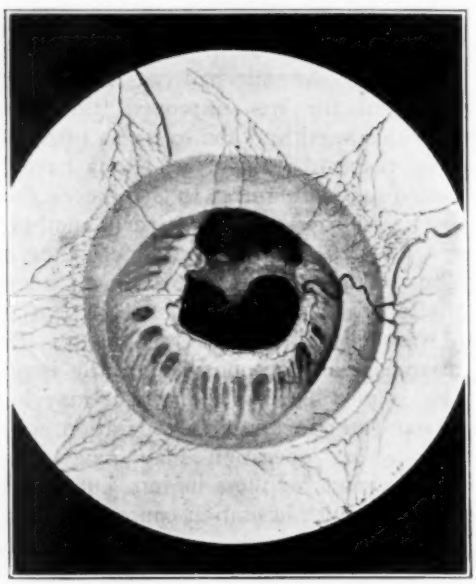

Fig. 3.—Artist's drawing of an eye in which the vascular connection between the iris and the episcleral net extends along the scar of an incision made for extraction of a cataract. This shows that if need for a newly formed vascular connection exists such a connection can be established along an operative wound.

is applied to the eye, and on the fifth day the suture is removed.

No eyes that have had this operation performed on them have been obtained; it is impossible to state whether or not new vascular connections are actually produced. In 1 instance, however, I have seen a vascular connection between episcleral vessels and newly formed vessels on the iris along the tract of an incision made for extraction of a cataract in a patient with severe glaucoma (fig. 3). This demonstrates that new vascular connections large enough to be seen without magnification can be and are established along an operative wound between the interior and the exterior of the eye if the need is strong enough.

SUMMARY

In approximately 12 per cent of all premature infants weighing 3 pounds (1,307 Gm.) or less at birth retrolental fibroplasia develops.

Partial resolution of the fibroplastic tissue in the eyes in which growth does occur when no complications arise rarely results in improvement sufficient to permit good vision.

Occasionally, cataractous development may obscure deeper ocular changes.

Inability of the infants to judge distance is a common characteristic.

The "fetal blue" color of the iris persists longer, its speed of disappearance being in direct proportion to the rapidity of growth of the involved eye.

One atypical case originally reported must now be excluded. The full term birth of a younger sister with the same lesion indicated a probable hereditary factor, not evident in any other cases.

Mental retardation in infants with retrolental fibroplasia appears to be less frequent than mental retardation in normal premature infants.

Radiation therapy has proved to be valueless, in fact, more damaging than beneficial.

Glaucoma, a complication of some frequency, rarely gives rise to hydrophthalmos and appears to be preventable by daily use of miotics. On the other hand, mydriatics having an effect of short duration used once a week are less successful in preventing posterior synechia.

The "dentate processes," originally improperly interpreted, are actually brown (pigmented) or red (unpigmented) ciliary processes, observable through dilated pupils, extending in front of the opaque tissue. These processes in infants with fibroplasia are narrower, often less pigmented and perhaps more elongated than the ciliary processes observed in the same manner in infants with normal eyes.

The more tenable theory of the cause of this disease is that failure of production or accumulation of aqueous humor may be caused by the effect of precocious exposure to light, which activates the musculature of the pupillary and the ciliary body before the hyaloid vascular system has disappeared. This failure leaves the crystalline lens dependent on the hyaloid artery and tunica vasculosa lentis, thereby causing persistence of this vascular system.

Surgical attempt to establish new vascular connections between the ciliary body and the episclera by scleral trephination over the ciliary body appears to produce some improvement.

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TWO UNUSUAL OCULAR TUBERCULOMAS

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The rarity of primary tuberculosis of the bulbar conjunctiva justifies the description of a case of this condition. The second case described in this article is an instance not of primary tuberculosis but of the formation and spread of a tuberculoma which are unusual and worthy of record.

The incidence of primary tuberculosis of the conjunctiva varies from 1:3,000 to 1:60,000 cases, of which 20 to 30 per cent are instances of the bulbar variety.[1] It is difficult to ascertain whether a tuberculous focus is primary or not. It is a general rule, originating from Axenfeld,[2] that progressive pulmonary tuberculosis is antagonistic to the establishment of tuberculosis in the eye. The cutaneous reaction to tuberculin is not entirely specific or dependable, for in some cases of proved tuberculosis the reaction is negative and a positive cutaneous reaction has been described in some cases in which no tuberculosis was present.[2] In our opinion, a positive reaction to an intradermal test with 1:5,000 dilution of old tuberculin is still a useful indication of the state of allergy or anergy of a person. A further useful sign is that with primary conjunctival tuberculosis there is usually early involvement of the regional lymph glands.[3] A few diagnostic signs in our first case point to the fact that the tuberculoma of the conjunctiva was primary in origin.

REPORT OF CASES

CASE 1.—A South African Negro 25 years of age was admitted to the hospital with a note from his physician which stated that the patient while hammering on rock during gold-mining operations sustained a horizontal laceration of the bulbar conjunctiva three weeks before we saw him. A tumor developed over the site of injury, and because there was enlargement of the preauricular and premasseteric lymph glands, his physician thought it might be malignant. On examination there was found a roll-like, somewhat pedunculated, red tumor lying horizontally below the cornea and attached to the scleral conjunctiva (fig. 1). It was vascular, resembling a glaucoma, and the conjunctiva around it was moderately hyperemic. The surface of the tumor was smooth, and no sign of ulceration existed. The premasseteric and preauricular lymph nodes were enlarged, hard and painful when palpated. On attempting to remove a piece of the tumor for histologic examination, we found that the entire tumor could be torn off at its base. The raw area, where it had been attached, was cauterized by heat, and it healed without any untoward reaction. The lymph glands were left untouched. Histologic examination revealed that the biopsy material consisted of tuberculous granulation tissue, and an intradermal test with a 1:5,000 dilution of old tuberculin was immediately carried out.

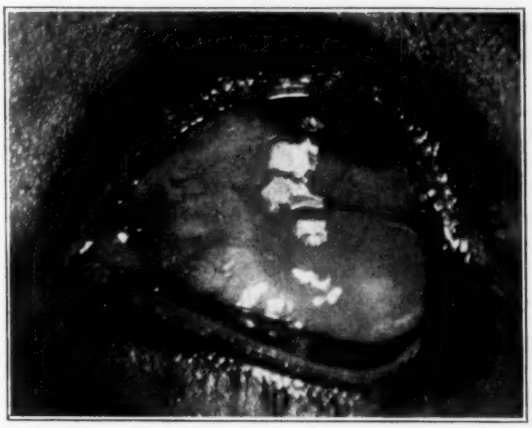

Fig. 1.—A primary tuberculoma of the bulbar conjunctiva.

This was repeated a week later. Both tests gave negative results. A biologic test with material from the preauricular lymph gland gave positive results. Roentgenologic examination of the lungs and investigation of the sputum yielded nothing of importance. During the fifth week after the patient was admitted to the hospital the intradermal test with old tuberculin gave a strongly positive result. At no time was there a rise in temperature or any loss of weight. The patient was treated with a tubercle endotoxoid prepared by the method of Grasset.[4] During the two months of endotoxoid treatment[5] the enlargement of the premas-

1. Samuelson, A.: Primary Tuberculosis of Conjunctiva, Arch. Ophth. **15**:975 (June) 1936.

2. Wegner, W.: Zeitfragen der Augenheilkunde, Stuttgart, Ferdinand Enke, 1938, p. 328.

3. Igersheimer, J., in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1932, vol. 7, p. 87.

4. Grasset, E.: Tubercle Endotoxoid in the Treatment of Tuberculosis in South African Natives, Am. Rev. Tuberc. **49**:1, 1944.

5. A full consideration of our results with tubercle endotoxoid treatment in ophthalmology will be the subject of a publication in the near future.

seteric and preauricular glands slowly disappeared. The patient was discharged as cured after three months in the hospital.

In this case primary infection of the bulbar conjunctiva entered through a conjunctival wound. As this South African native is a worker in a gold mine, where he is exposed to tuberculous infection, such an entrance of the bacillus is feasible.

Case 2.—In a South African Negro, approximately 40 years of age, a large, smooth, flattish, rounded tumor developed subconjunctivally on the sclera under the upper eyelid (fig. 2). It is not known how long this growth had existed before his physician discovered it. The tumor caused no vascular reaction in the overlying conjunctiva. The eye itself showed signs of long-standing chronic iridocyclitis; posterior synechiae and abundant keratic precipitates were present. Gonioscopically we could find only abnormal deposition of fine brown pigment on the iridocorneal trabecula and deposition of fibrinous masses central to the internal corneal bulge of Schwalbe. The lens was slightly hazy, but the vitreous was so cloudy that only an indistinct glimpse of the choroid of the lower quadrants of the fundus could be obtained. Roentgenologic and laboratory investigations gave negative results; there was mild lymphocytosis, and an intradermal test with 1:5,000 dilution of old tuberculin gave strongly positive results. Biopsy was thought necessary. Through a small conjunctival incision, a piece of the granuloma was excised, and at once vitreous humor appeared at the site. The conjunctiva was immediately sutured. It was now obvious that the vitreous protruded beyond its normal limits because of erosion of the coats of the eye. During the three weeks following the operation the eye became inflamed and hypotonic, owing to advanced destruction of the uvea and reaction resulting from operative intervention. We instituted endotoxoid treatment, but it was already too late. After three weeks in the hospital the patient refused further treatment and at his insistence was repatriated to Portuguese East Africa. The pathologist reported that in the tuberculous granulation mass traces of choroid and sclera were present. No biologic test was made.

Fig. 2.—Subconjunctival protrusion of a uveal tuberculoma.

This tuberculoma could not have been primary in origin but must have been a blood-borne infection from some unknown source. What is interesting is the fact that the tumor eroded the coats of the eye and grew outward under the conjunctiva.

INTRAVITREAL PENETRATION OF PENICILLIN AND PENICILLIN THERAPY OF INFECTIONS OF THE VITREOUS

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Recently von Sallmann, Meyer and Di Grandi [1] have pointed out the unsatisfactory response of ectogenous infections of the vitreous to any type of therapy. Von Sallmann [2] demonstrated that iontophoresis with penicillin and iontophoresis plus systemic administration of sulfonamide compounds failed to produce improvement of ectogenous intraocular infections. Because these authors were unable to produce adequate levels of penicillin in the vitreous of the normal eye by corneal iontophoresis or by systemic administration, they resorted to direct intravitreal injections. Their studies showed that penicillin was present in the vitreous humor in a concentration greater than the bacteriostatic requirement for twenty-four hours after the initial injection. Initial intravitreal injections of penicillin produced retinal damage at the site of the needle puncture and opacities and occasional hemorrhage in the vitreous. The authors stated that if a fine needle was used and directed into the central area of the vitreous there was little danger of producing a cataract or retinal detachment with one injection of refined penicillin.

Von Sallmann, Meyer and Di Grandi [1] did not study the histologic damage following intravitreal injection of sulfonamide compounds. Leopold and Scheie [3] briefly reported such changes following intravitreal injection of sulfanilamide, sulfapyridine and sulfathiazole. The histologic damage brought about by such injections was similar to that observed with penicillin and was most pronounced with sulfapyridine. Leopold and Scheie [3] suggested that there was little to be gained by intravitreal injections of sulfonamide compounds, as theoretically quite adequate concentrations in the vitreous could be obtained in infected eyes by systemic administration of these substances. They suggested that the only gain from such treatment would be an immediately high intravitreal concentration of the agent. The failure of intravitreal injections of the sulfonamide compounds to be more effective than the systemically administered drug in clearing infections with Staphylococcus aureus, as reported by von Sallmann, Meyer and Di Grandi,[1] substantiates this impression. These authors were able to halt the progress of infections of the vitreous with a hemolytic strain of Staph. aureus by means of one intravitreal injection of a solution of penicillin. As already pointed out, their reasons for adopting this method of therapy were based on the inadequacy of concentrations in the vitreous obtained in the normal eye with less damaging routes of administration. It seemed advisable, therefore, to determine the vitreous concentrations to be obtained in the inflamed eye by intramuscular, intravenous and subconjunctival injections and by injection into the anterior chamber.

It is to be expected that with increased permeability of the capillaries there might be an increased penetration of penicillin into the vitreous. An increase in the secondary aqueous has been shown to follow systemic administration of penicillin after paracentesis by von Sallmann and Struble and Bellows [4] and after inflammation by Leopold and LaMotte.[5]

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1. von Sallmann, L.; Meyer, K., and Di Grandi, J.: Experimental Study on Penicillin Treatment of Ectogenous Infection of Vitreous, Arch. Ophth. **32**:179 (Sept.) 1944.

2. von Sallmann, L.: Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infection with Pneumococcus, Arch. Ophth. **30**:426 (Oct.) 1943.

3. Leopold, I. H., and Scheie, H. G.: Studies with Microcrystalline Sulfathiazole, Arch. Ophth. **29**:811 (May) 1943.

4. Struble, G. E., and Bellows, J. G.: Studies on the Distribution of Penicillin in the Eye, J. A. M. A. **125**:685 (July 1) 1944.

5. Leopold, I. H., and LaMotte, W. O., Jr.: Penetration of Penicillin in Rabbit Eyes with Normal, Inflamed and Abraded Corneas, Arch. Ophth. **33**:43 (Jan.) 1945.

PENETRABILITY OF PENICILLIN INTO THE VITREOUS

Methods of Administration.—The following routes of administration were considered in this study:

1. Subconjunctival injection consisting of 0.25 cc. of a solution containing 10,000 Oxford units of sodium penicillin per cubic centimeter[6] of isotonic solution of sodium chloride U. S. P. Such injections were made in eyes previously anesthetized with a 0.5 solution of tetracaine hydrochloride.

2. Intramuscular injection of 4,000 Oxford units of sodium penicillin per kilogram of body weight.

3. Intramuscular injections of 4,000 Oxford units of penicillin[7] per kilogram of body weight. This solution of penicillin also contained naphthylmethylimidazoline hydrochloride,[8] 0.25 mg. per cubic centimeter, or neo-synephrine hydrochloride, 0.5 mg. per cubic centimeter, and 20 or 6 per cent gelatin, the concentration depending on the vasoconstrictor used. Such preparations have been shown by Rhoads and his associates[9] to maintain high levels of the substance in the blood for several hours. This method was tried here with the hope that the prolonged level of the substance in the blood would allow greater penetration into the vitreous humor.

4. Intravenous injections of penicillin. Each injection contained 4,000 Oxford units of the sodium salt per kilogram of body weight.

5. Injections into the anterior chamber of 0.25 cc. of a solution containing 2,000 units of sodium penicillin per cubic centimeter. The anterior chamber was punctured obliquely, starting at the limbus in eyes previously anesthetized with a 0.5 per cent solution of tetracaine hydrochloride. The aqueous humor was withdrawn into the syringe and mixed with the penicillin solution in the syringe. Then 0.25 cc. of the mixture of penicillin solution and aqueous humor was injected into the anterior chamber. The resultant solution injected contained approximately 250 Oxford units of penicillin. Although the punctures were made obliquely through the cornea, some of the aqueous mixture leaked from the puncture site; so the exact amount in the anterior chamber was not known. All concentrations of penicillin were determined by a modification of Rammelkamp's method of bioassay.[10]

Studies were made on the following types of rabbit eyes:

1. Normal rabbit eyes.

2. Rabbit eyes with infections of the anterior chamber. The infections were produced by injection of 0.02 cc. of a diluted eighteen hour broth culture of a hemolytic strain of Staph. aureus. Each injection contained approximately 400 organisms. One could not be certain of the exact amount of culture retained in the anterior chamber, as some aqueous humor always leaked out of the puncture. However, in all eyes so treated signs of severe infection developed within twenty-nine hours; these eyes were anesthetized with a 0.5 per cent solution of tetracaine hydrochloride prior to injection of the culture. Penicillin studies were made twenty-four hours after such injections.

3. Rabbit eyes with 0.02 cc. of histamine hydrochloride (1:1,000) injected into the vitreous fifteen minutes before administration of any penicillin preparation. All eyes were locally anesthetized with a 0.5 per cent solution of tetracaine hydrochloride.

4. Rabbit eyes on which basal iridectomies were done two weeks prior to any penicillin studies. Approximately one fifth of the iris was removed in this operation.

In all instances, the specimens of vitreous were analyzed fifteen minutes, forty-five minutes and one hour and forty-five minutes after the initial administration of penicillin. After some modes of administration it was necessary to determine the concentrations of penicillin in the vitreous three hours and four hours after injection.

TABLE 1.—*Intravitreous Concentrations of Penicillin Following Intramuscular and Intravenous Administration of Penicillin*

Method of Administration	Time of Analysis After Administration, Min.	Normal Eyes, Oxford Units of Penicillin per Cc.	Eyes with Infections of Anterior Chamber, Oxford Units of Penicillin per Cc.	Eyes with Intravitreous Histamine, Oxford Units of Penicillin per Cc.
Intramuscular, 4,000 units/Kg.	15	0	0	0
	45	0	0.03	0
	105	0	0.03	0
Intramuscular, 4,000 units/Kg. (+ gelatin and vasoconstrictor substance)	15	0	0	0
	45	0	0	0
	105	0	0.03	0.02
	180	0	0	0
	240	0	0	0
Intravenous, 4,000 units/Kg.	15	0	0	0
	45	0	0.03	0
	105	0	0.07	0.02
	180	0	0.01	0

Results.—The data are listed in tables 1, 2 and 3. All levels represent the average levels for the two eyes. It is evident from the data listed in table 1 that detectable concentrations of penicillin in the vitreous were not present in normal eyes after intravenous or intramuscular administration of penicillin. These results also indicate that prolongation of the level of penicillin in the blood by use of a penicillin-gelatin-vasoconstrictor preparation did not increase the penetration of penicillin into the vitreous of normal eyes. In eyes with infections of the anterior segment the penicillin did penetrate into the vitreous humor with all these methods. Intravenous injection produced the

6. The penicillin was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for clinical investigations recommended by the Committee on Chemotherapeutics and other agents of the National Research Council.

7. This preparation of penicillin was supplied by Dr. William Parkins, of the Harrison Department of Surgical Research of the Hospital of the University of Pennsylvania.

8. This compound was obtained in the form of privine hydrochloride (Ciba Pharmaceutical Products, Inc.).

9. Rhoads, J. E., and others: Personal communication to the author.

10. Rammelkamp, C. H.: Methods for Determining Concentration of Penicillin in Body Fluids and Exudates, Proc. Soc. Exper. Biol. & Med. **51**:95 (Oct.) 1942.

highest levels of penicillin in the vitreous. Penicillin in the vitreous was just detectable in eyes which had received intravitreous injections of histamine prior to administration of the penicillin.

The results of subconjunctival administration of penicillin are recorded in table 2. Although the presence of the substance in the vitreous was detectable in normal eyes for three hours after such an injection, the levels were much greater in eyes with an inflamed anterior chamber. Even in normal, as well as in inflamed eyes, subconjunctival injection produced higher intravitreal levels than the intramuscular or the intravenous mode of administration.

TABLE 2.—*Intravitreous Concentrations of Penicillin Following Subconjunctival Injections of Penicillin*

Time of Analysis After Injection, Min.	Normal Eyes, Oxford Units of Penicillin per Cc.	Eyes with Infections of Anterior Chamber, Oxford Units of Penicillin per Cc.
15	0.000	0.128
45	0.078	0.510
105	0.078	0.250
180	0.078	0.250

The results of injections into the anterior chamber are presented in table 3. The concentrations in the vitreous of normal eyes were greater than the concentrations obtained by any previous method. The levels obtained in inflamed eyes were still greater. In eyes which were normal except for previous iridectomy, the vitreous level exceeded that in the vitreous of normal eyes similarly treated with injections into the anterior chamber.

TABLE 3.—*Intravitreous Concentrations of Penicillin Following Injections of Penicillin Into Anterior Chamber*

Time of Analysis After Injection, Min.	Normal Eye, Oxford Units of Penicillin per Cc.	Eyes with Infection of Anterior Chamber, Oxford Units of Penicillin per Cc.	Eyes with Iridectomy, Oxford Units of Penicillin per Cc.
15	0.312	0.624	0.312
45	0.312	1.200	0.312
105	0.312	0.624	0.624
180	0.078	0.312	0.312
240	0.039	0.078	0.624

In a recent review, Salter [11] has indicated that a desirable concentration of penicillin in the blood would be in the range of 0.15 Oxford unit per cubic centimeter. Theoretically, therefore, all the methods described which produce intravitreous levels in excess of 0.15 Oxford unit per cubic centimeter might be of value in treating infections of the vitreous due to penicillin-sensitive organisms. The methods which produce levels of 0.15 Oxford unit per cubic centimeter of vitreous or higher in infected eyes merit trial in treatment of infections of the vitreous. Subconjunctival injection and injection into the anterior chamber produced levels in the vitreous above 0.15 unit per cubic centimeter in eyes with an inflamed anterior segment. The parenterally administered penicillin never reached this concentration in the vitreous. Intravenous administration of penicillin produced a concentration of penicillin in the vitreous of about 0.08 unit per cubic centimeter in the inflamed eye. This was the highest level reached with the parenteral method of administration. These methods were therefore compared with the intravitreal injection of penicillin for effectiveness in combating an experimental ectogenous infection of the vitreous.

11. Salter, W. T.: Antibiotics and Bacteriostatics in Blood and Body Fluids, New England J. Med. **231**: 651 (Nov. 9) 1944.

PENICILLIN THERAPY OF INFECTIONS OF VITREOUS

Method.—All rabbits were of a blue-eyed or brown-eyed chinchilla strain, weighing between 2 to 3 Kg. The organism used was Staph. aureus, taken from a patient with septicemia. An eighteen hour culture of this organism was sensitive to concentrations of penicillin in the serum ranging from 0.05 to 0.02 Oxford unit per cubic centimeter. Intravitreous injections of 0.01 cc. of a diluted eighteen hour broth culture of this organism were made in both eyes of 50 rabbits. Each injection contained approximately 400 organisms. In all eyes receiving such injections signs of severe infection developed in twenty-four hours. By that time aqueous flare and floaters were conspicuous. The vitreous gradually became opaque, preventing any detailed view of the fundus. All untreated eyes were phthisical after four to six weeks. Treatment was started in all rabbits two hours after injection of the culture of Staph. aureus. The following methods of treatment with sodium penicillin were used:

1. Intravenous administration of 4,000 Oxford units of penicillin per kilogram of body weight. Injections were made every two hours and were continued for seventy-two hours. Six rabbits were used.

2. Subconjunctival injections of 0.25 cc. of a solution containing 10,000 Oxford units of penicillin per cubic centimeter. These injections were made every three hours for seventy-two hours. The previous determinations of intravitreal concentrations indicated that one such injection maintained concentrations above 0.20 Oxford unit per cubic centimeter for three hours. The right eyes of 6 rabbits were so treated, the left eyes receiving no therapy.

3. Injections into the anterior chamber of 0.25 cc. of a solution containing 2,000 units of penicillin per cubic centimeter. These injections were made in a manner similar to the injections described in the first part of this paper. According to the intravenous levels of penicillin obtained, one such injection maintained the intravitreal concentration of penicillin above 0.3 Oxford

unit for three hours. Therefore injections were made every three hours. Although care was exercised not to touch the lens with the needle, considerable damage to the lens occurred in 3 eyes so treated. Occasional hemorrhage occurred in the anterior chamber, and considerable fibrinous exudate appeared in all eyes, which made repeated injections difficult and inconstant in amount. This method of therapy was continued for seventy-two hours. The right eyes of 6 rabbits were so treated, the left eyes receiving no therapy.

4. Intravitreal injections of 0.25 cc. of a solution of penicillin containing 10,000 Oxford units per cubic centimeter of isotonic solution of sodium chloride. The cornea became hazy after each such injection, owing to the increase of intraocular tension, but cleared within a short while as some fluid leaked from the puncture site. All injections were made after anesthetizing the eye with a 0.5 per cent solution of tetracaine hydrochloride. These injections were made into the center of the vitreous, care being taken to avoid making contact with the lens. The right eyes of 6 rabbits were so treated, the left eye of each animal receiving no therapy.

5. Intravitreal injections of penicillin of various concentrations. Two right eyes received 2,000 units per injection; 2 right eyes, 1,000 units per injection; 2 right eyes, 500 units per injection; 2 right eyes, 250 units per injection; 4 right eyes, 100 units per injection; 2 right eyes, 50 units per injection; 2 right eyes, 25 units per injection; 2 right eyes, 10 units per injection, and 2 right eyes, 5 units per injection. All 20 left eyes received no therapy and acted as controls.

6. Injections into the anterior chamber of 0.25 cc. of isotonic solution of sodium chloride. Injections were made in six right eyes every three hours for seventy-two hours.

7. Intravitreal injection of 0.25 cc. of isotonic solution of sodium chloride. One injection was made in each of 6 eyes.

Results of Therapy.—All the 38 left eyes which received no therapy showed pronounced softening and opacity of the vitreous in four weeks. The 6 eyes which received injections of isotonic solution of sodium chloride into the anterior chamber and the 6 eyes which had intravitreal injections of isotonic solution of sodium chloride also were phthisical after four weeks of observation. All 12 eyes treated with intravenously administered penicillin showed all the signs of phthisis bulbi after four weeks. Four of the eyes which received subconjunctival injections appeared similar to the control eyes, while 2 of these eyes showed posterior cortical opacities of the lens, prominent opacities of the vitreous and a partial view of the fundus after four weeks. The inflammatory process was arrested in these 2 eyes, but no further clearing occurred in the subsequent ten weeks of observation. One of the eyes treated with injections into the anterior chamber showed only a few vitreous and lenticular opacities, and most of the fundic details could be seen after four weeks. One eye so treated allowed a partial view of the fundus. Posterior synechiae were present in this eye, as well as lenticular and large vitreous opacities. The intraocular tension, however, was maintained. The remaining 4 eyes showed phthisis bulbi at the end of four weeks.

All 6 eyes treated with injections of 2,500 Oxford units of penicillin were quiet after four weeks of observation. Occasional opacities in the vitreous, but no other sign of inflammatory activity, could be seen in all the eyes. Of the 20 eyes treated with decreasing doses of penicillin by injection into the vitreous, all receiving more than 1,000 units per injection were favorably influenced, in a manner similar to the eyes treated with 2,500 units per injection.

One eye each of the eyes receiving injections of 500 and 250 units into the vitreous also appeared similar to the eyes receiving 2,500 units per injection. All the remaining eyes showed considerable opacification of the vitreous, lenticular opacities and posterior synechiae. A partial view of the fundus could be obtained in these eyes, and the intraocular tension was maintained in the other eye which received 250 units, in 2 of the 4 eyes which received 100 units and in 1 each of the eyes receiving 50, 25, 10 and 5 units per injection. Even in the poorest of the last-mentioned eyes the inflammatory process was never as severe, nor did the eyes progress as rapidly to the end stages, as in the untreated controls.

COMMENT

It is evident that subconjunctival injection and injection into the anterior chamber will produce theoretically adequate concentrations of penicillin in the vitreous in inflamed rabbit eyes. Administration of 4,000 units of penicillin per kilogram by the intravenous or by the intramuscular route does not. When these methods are tried against a standard ectogenous infection of the vitreous produced by a highly susceptible strain of Staph. aureus, subconjunctival injection of penicillin and injection into the anterior chamber have some success in combating the infection. This success is not striking even when therapy is started two hours after inoculation of the vitreous with the organisms. Intravitreal injections were successful in all cases when the concentration of penicillin was above 500 Oxford units per injection. Even lower concentrations, as small as 5 Oxford units per injection, had some effect. Thus intravitreal injections are superior in therapeutic efficiency to subconjunctival injection and injection into the anterior chamber. However, both methods have some

merit, whereas all methods of systemic administration fail entirely.

Injections into the anterior chamber in themselves produce considerable disturbance in the aqueous. Dunnington and von Sallmann [12] showed that one such injection produces reparable changes. However, repeated injections of penicillin produced some irreparable damage in the present experiments. Lenticular opacities and anterior and posterior synechiae occurred. Much of this damage may be mechanical in origin, as the eyes which received repeated injections of isotonic solution of sodium chloride into the anterior chamber also showed lenticular damage and formation of synechiae. However, iontophoresis [2] and subconjunctival injections [4] also give high concentrations in the anterior chamber and should be used whenever possible in place of injections into the anterior chamber. Thus, unnecessary trauma to the intraocular structures of the anterior segment will be avoided.

These studies indicate that with increase in capillary permeability, such as occurs in eyes with intraocular inflammation, the penetration of penicillin into the vitreous is greater than the penetration of the substance into the vitreous of the normal eye when locally or systemically administered. The difference between the penetration of penicillin into the vitreous of normal eyes and the penetration into the vitreous of inflamed eyes is less than the difference in the concentration of penicillin reached in the aqueous of normal eyes and the concentration reached in the aqueous of inflamed eyes. The levels of penicillin in the vitreous of eyes with inflammation of the anterior segment following intramuscular administration, as recorded here, are considerably less than the concentrations observed by Leopold and La Motte [5] in the aqueous humor of eyes with corneal infections. Our observations are similar to those of Duke-Elder,[13] who stated that the vitreous resembles the aqueous in the quality of its changes in content secondary to alterations in capillary permeability but that the changes in the vitreous are smaller, take longer to reach a maximum and return more slowly to normal than do the changes in the aqueous. It has also been noted by many observers that the increase in capillary permeability is greater in the experimental animal, especially the rabbit, than in man.[13b] Therefore, although it is important to determine the concentration of penicillin in the vitreous of inflamed eyes before any method of therapy is recommended, the data reported here indicate that this concentration is not so important a factor in the case of the vitreous humor as in that of the anterior segment of the eye.

It is interesting to note that although high concentrations of penicillin are produced in the anterior chamber, relatively little penicillin reaches the vitreous chamber. This supports the belief that the iris-lens contact is fairly close and that the flow of substances in the anterior chamber is largely away from the vitreous.[13c] Adler's [14] studies with sugar indicated this. In this investigation he suggested that iridectomy might increase the concentration in the vitreous of substances placed in the anterior chamber. In the eyes with small iridectomies penicillin reached the vitreous from the anterior chamber in higher concentrations than it did in normal eyes. This study suggests that corneal iontophoresis or injection of penicillin into the anterior chamber might give adequate concentrations of the substance in the vitreous in eyes with iridectomy, aphakia or partial or complete removal of the lens-iris barrier. Dunnington and von Sallmann [12] reported 3 cases of endophthalmitis, probably due to Staph. aureus, in aphakic eyes. In these cases penicillin iontophoresis was used, with successful regression of the infection in 1 case, with regression but loss of visual ability in another and with total failure in the third.

It is tempting to speculate on the reason for the failures of subconjunctival injection and injection into the anterior chamber to control successfully experimental infection in all cases reported here, even though these methods produce theoretically adequate concentrations of penicillin in the vitreous of the inflamed eye. It may be that the penicillin diffuses slowly and unequally through the vitreous gel. It is also possible that the organism is not so susceptible to penicillin in the vitreous gel as in serum or aqueous humor. It may be that the infection was too overwhelming. However, it is important to note that these methods were partially successful in controlling the infection in 4 out of 10 eyes. One may conclude that methods of producing high concentrations of penicillin in the anterior chamber, such as iontophoresis [2] and injections into the anterior chamber, as well as subconjunctival injections,[4] have merit in treating ectogenous infections of the vitreous due to a penicillin-sensitive organism. In the presence of a break in the lens-iris barrier, such methods may be more successful. However, no one of these methods

12. Dunnington, J. H., and von Sallmann, L.: Penicillin Therapy in Ophthalmology, Arch. Ophth. **32**:353 (Nov.) 1944.

13. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1939, vol. 1, (*a*) p. 466; (*b*) p. 441; (*c*) p. 468.

14. Adler, F. H.: Sugar Content of Ocular Fluids, Tr. Am. Ophth. Soc. **28**:307, 1930.

is as efficient as intravitreal injections of penicillin.

SUMMARY

1. Intramuscularly and intravenously administered penicillin in a concentration of 4,000 units per kilogram failed to produce detectable concentrations of penicillin in the vitreous humor in the normal rabbit eye.

2. Prolonging the length of time that penicillin remained in the blood stream by employing a penicillin-gelatin-vasoconstrictor preparation failed to increase the intravitreous penetration of penicillin from the blood stream in the normal rabbit eye.

3. Subconjunctival injection of penicillin and injection of the substance into the anterior chamber produced detectable concentrations of penicillin in the vitreous in the normal rabbit eye.

4. All methods of administration produced higher concentrations of penicillin in the vitreous humor in the rabbit eyes with infection of the anterior chamber than in normal eyes.

5. Theoretically adequate concentrations of penicillin in the vitreous were obtained with administration of penicillin by subconjunctival injection and by injection into the anterior chamber in the inflamed rabbit eye. Such levels were adequately maintained for three hours after one injection.

6. Higher concentrations of penicillin in the vitreous were obtained in eyes with iridectomies than in normal eyes after injections of penicillin into the anterior chamber.

7. Intravenously administered penicillin failed to stop the progression of experimentally induced ectogenous infections of a vitreous caused by a penicillin-sensitive strain of Staph. aureus.

8. Repeated subconjunctival injections of penicillin and injections into the anterior chamber halted the progress of intravitreal infection due to Staph. aureus in 4 of 10 rabbit eyes.

9. Intravitreal injections halted the progress of ectogenous infections of the vitreous due to Staph. aureus in all eyes receiving one injection consisting of more than 500 Oxford units of penicillin. Lower concentrations than this, including 5 units per injection, were partially successful.

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CYCLOPIA COMPLETA AND ARHINENCEPHALIA COMPLETA WITH UMBILICAL HERNIA IN A FULL TERM CHILD

REPORT OF A CASE

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Recently there came into my hands the case history and excellent photographs of a human monster at term with cyclopia completa, arhinencephalia completa and umbilical hernia. The materials were brought to me by Mr. Daniel B. Levy, a student in the University of Virginia Medical School, who obtained them through the courtesy of Dr. H. M. Digges, of Suffolk, Va., the attending physician. The specimen is of special interest because it was one of those extremely rare monsters in which there is absolutely no trace of a nose, and yet aside from this defect and the presence of the cyclopean eye the face shows only a slight degree of abnormality.

Hannover (1882) collected the reports of 103 cases of cyclopia in man which had been published up to that time.[1] Examination of the reference to cyclopia in man in the *Quarterly Cumulative Index Medicus* and in the "Index Catalogue of the Library of the Surgeon-General's Office of the United States Army" since that time has revealed 92 instances reported since 1882. This total of 195 cases is a rather low incidence of malformation compared with the incidence of malformation in other parts of the body. Thirty of these cases in which the anomalous conditions are well discussed and illustrated and which seem to be representative of the variations which accompany cyclopia have been used as a background in describing the present specimen.

HISTORY OF THE CASE

The father was 28 years of age; the mother, aged 25, had previously borne 2 normal living children. Both parents were Negroes. Wassermann tests gave negative reactions. Both parents said they had not had any venereal disease. The mother suffered severe suprapubic pain during the last three months of pregnancy. There was no evidence of toxemia before, during or after delivery. The recovery was normal. Labor began at term and lasted from 10 a. m. to 10 p. m. The child was born in the left occipitoanterior position.

The child, who was thought to be female, weighed 10 pounds 2½ ounces (5,775 Gm.). There was four or five times the usual amount of amniotic fluid. The only signs of life were a few muscular movements, which subsided practically at once. There was no evidence that the lungs were ever expanded. The body was covered with a persisting lanugo, and the hair on the head was excessively long. There was no nose. A single eye was present in the center of the face. The eye was open at birth and remained so. A mouth was present. The limbs and feet were symmetric and of normal shape, but rather short and stubby. There was a large umbilical cord, into the base of which there was a definite umbilical hernia, with viscera protruding into the sac. Necropsy was not permitted.

DESCRIPTION OF THE SPECIMEN AND COMMENT

The statements just given were made by Dr. Digges. Although a necropsy was not performed and the internal anatomy could therefore not be examined, the unusual nature of the specimen seems to warrant recording. The pictures shown in the text were taken immediately after birth and are clear enough to permit amplification and interpretation of the facts supplied by Dr. Digges.

A photograph of the whole body is shown in figure 1. The child is large—probably the largest on record with a cyclopean eye. In 16 cases of cyclopia in which the weight at birth of the specimen was given, the range was from 1,075 to 3,750 Gm. (average weight 2,000 Gm.). Most of the cyclopean monsters have been premature babies of the seventh or eighth month.

In 17 cases in which observations were made of the viability of the child at birth 9 babies were stillborn, of whom 4 were viable up to the time of birth and 2 lived for fifteen minutes, 2 for one-half hour and 4 for one hour, two hours, three hours and four hours respectively. It is generally agreed that there is no reliable record of survival of a human cyclopean monster for any great length of time. Hence the paucity of signs of life exhibited by this specimen is not unusual.

The presence of a greater amount of amniotic fluid than is normal suggests that hydramnios was present. Such a condition is not unusual in human cyclopia, since in 16 cases from the modern literature in which histories of the conditions at birth were given hydramnios was present in

1. Hannover, A., cited by Adelmann.[34]

6 cases, or 37 per cent. Such an incidence of hydramnios is significantly greater than in single births from unselected populations, where it has been estimated to be about 0.5 to 1.0 per cent.[2] The etiologic significance of hydramnios in relation to cyclopia has not been explained, but it might be suggested that hydramnios is an expression of general physiologic disturbance in the environment in which the embryo has developed.[3] This state of the environment may also be related to the age and condition of parity in the mother, since in 15 cases for which the latter information was given no mother was younger than 27 years and there were only 2 primiparas.

Fig. 1.—The cyclopean monster as viewed from the right side to show the size and position of the umbilical hernia. (Photograph by Gerald Rose.)

The proportions of the body of the monster are in general normal, but there is a tendency toward shortness of limbs and digits. The umbilical hernia is the most striking abnormality of the body aside from those of the face. The position, size and shape of the hernial sac are well shown in figure 1. The viscera protrude into a translucent membranous sac at the base of the umbilical cord. This sac consists of the amnion fused with a remnant of the original wall of the embryophore. The nipple-like structure at the right of the mass is a small piece of protruding intestine. This malformation has been reported in human cyclopean monsters, according to Chidester [4] and Ognew,[5] but I have found no reference to it in the modern literature. Ognew interpreted umbilical hernia and other malformations which have been reported to accompany cyclopia as evidence for the centrifugal spreading of biologic agents of destruction. He expressed the opinion that malformations may be attributed to developmental disturbance of the formative cells from which the embryo differentiates. The greatest modifications of development take place in a weak central region, such as the cephalic end of the body, and from there may spread peripherally and not only radically alter normal development but affect detrimentally cells or organs which hitherto have been completely normal.

The external genitalia in this specimen do not appear to be normal. From the immediate examination Dr. Digges thought they were female, but if this is the case the condition apparent in the photograph indicates that the clitoris is larger than normal. The alternative is incomplete development of the labioscrotal swellings and hypospadias, conditions which cannot be decided by examination of the picture. Abnormalities of the external genitalia, particularly in female cyclopeans, have been reported, but in descriptions of 30 representative cyclopeans there are only 2 references to malformed genitalia, and in both of these specimens the organs were undeveloped male organs.[6]

The excellent photograph of the face as viewed from the front (fig. 2) allows a more detailed examination of the features. The head is set squarely on the shoulders, and there is little if any neck. The back of the head is much broader than the face and can be seen bulging behind the ears. In 8 of the representative 30 specimens to which I referred the head was so set on the shoulders. In the present specimen the whole top and back of the head are covered with long black hair, which extends down on the front of the head almost to the eye. Specific mention of long hair extending down on the

2. Szendi, B.: Ueber die Bedeutung der Struktur der Eihäute und des Gefassnetzes der Placenta auf Grund von 112 Zwillungsgeburten, Arch. f. Gynäk. **167**:108 (May) 1938.

3. Mall, F. P.: A Study of the Causes Underlying the Origin of Human Monsters, J. Morphol. **19**:3 (Feb.) 1908.

4. Chidester, F. E.: The Origin of Cyclopean Monsters, Am. Nat. **57**:496 (Nov.-Dec.) 1923.

5. Ognew, B. W.: Die Zyclopie im Zusammenhang mit Anomalien anderer Organe, Anat. Anz. **70**:241 (Sept.) 1929.

6. (*a*) Burns, W.: Cyclopean Monstrosity, Boston M. & S. J. **68**:513 (July 30) 1863. (*b*) Chapman, K. H.: Human Cyclopia, Arch. Ophth. **16**:40 (July) 1936.

forehead has been made in several descriptions,[7] and in practically all of the pictures from the most recent literature the hair seems to be more profuse than in normal newborn children.

There is practically no forehead, a characteristic common to most cyclopeans. On the margins of the space immediately above the eye are the rudiments of eyebrows or superciliary ridges, which are separated from each other in the middle line and which extend over the lateral margins of the eye at an angle of about 45 degrees. These partial eyebrows are covered with long hairs which extend laterocephalad at right angles to the direction of the ridges. The point at which each eyebrow ends medially seems to be at the region of the supraorbital notch. Such partial eyebrows in cyclopeans have been recorded by several investigators.[8] In a normal embryo of 16 mm. the lower lid on each side is already formed as a shelflike process of the maxillary process below the eyeball. Medially it meets the lateral nasal process in the naso-optic groove. The upper lid and the eyebrows start at this time, each as a lateral fold of mesoderm covered with ectoderm which grows first laterally from the supraoptic region and forms the outer canthus.[9] At the 18 mm. stage a new fold appears medial to this and joins the lateral fold to complete the median part of the upper lid and the eyebrow. From such a normal condition it could be inferred that the cyclops lacked not only the primordium of a nose but also that part of the mesoderm which forms the median parts of the eyebrows and the upper lids. The lateral parts did develop, and hence the rudiments of eyebrows. There is the possibility that the lateral parts of the eyebrows and the upper lids are proliferated from the mesoderm of the laterocephalic margin of the maxillary processes, which are undergoing rapid extension at the time the eyelids are forming.

Fig. 2.—A front view of the face of the cyclopean monster. (Photograph by Gerald Rose.)

Below the superciliary ridges and the limited central region of the forehead there is a single superior palpebra arching over the open palpebral fissure. This eyelid has no trace of a tarsal arch, and the palpebral fold ends abruptly at the outer canthus, where its lateral margins are overlapped from below by the inferior palpebra. There are suggestions of cilia on the margins, but they are not marked. The inferior palpebrae are only slightly arched, and the two lateral components meet medially at a notch. Each side of the notch meets the lid at an angle characteristic of the normal inner canthus. No puncta lacrimalia can be seen, and there seems to be no trace of cilia, but the lateral ends of the inferior palpebrae appear to have each a tarsal arch.

Of 25 representative specimens of cyclopia, 14 had a single arch formed by the superior palpebra similar to that just described, although not always with the same degree of arching.[10]

7. (*a*) Allan, R.: A Human Astomatous Cyclops, Lancet **1**:227 (Feb. 26) 1848. (*b*) Hall, A. D.: Case of Cyclopic Malformation, Boston M. & S. J. **65**:263 (Oct. 24) 1862. (*c*) Smith, S., and Boulgakow, B.: A Case of Cyclopia, J. Anat. **61**:105 (Oct.) 1926.

8. (*a*) Hall.[7b] (*b*) Smith and Boulgakow.[7c] (*c*) Allen, F. H.: Cyclopia, M. Rec. **50**:249 (Aug. 15) 1896. (*d*) Dougal, D., and Bride, T. M.: A Case of Cyclopia, Brit. M. J. **2**:13 (July 4) 1914. (*e*) Best, E.: Zur Frage der Cyclopie und Arhincephalie, Beitr. z. path. Anat. u. z. allg. Path. **67**:437, 1920. (*f*) Hagens, E. W.: Unilateral Malformation of the Ear Associated with Cyclopia, Arch. Otolaryng. **18**:332 (Sept.) 1933. (*g*) Breckwoldt, H.: Ueber die Zahnverhältnisse bei Zyklopie und Gesichtsspaltes, Beitr. z. path. Anat. u. z. allg. Path. **98**:115 (Dec.) 1936.

9. Mann, I. C.: The Development of the Human Eye, London, Cambridge University Press, 1928.

10. (*a*) Burns.[6a] (*b*) Chapman,[6b] case 3. (*c*) Allan.[7a] (*d*) Smith and Boulgakow.[7c] (*e*) Dougal and Bride.[8d] (*f*) Best.[8e] (*g*) Hagens.[8f] (*h*) Scott, J.: A Monoculous Male Foetus, Lancet **1**:633 (June 14) 1862. (*i*) Koogler, M. A.: A Report of Three Human Mon-

(Footnote continued on next page)

Such a morphologic relation is the result of the failure of the median primordia of the upper lids to form. In 9 specimens these primordia had formed, and the upper lid was composed of two parts which met at a notch in the middle line.[11] In 2 specimens in which only a rudimentary eye was present the palpebral fissure was a mere slit.[12]

There was only a single specimen in this group with an eyeball in which the inferior palpebrae were undivided.[10b] In 22 specimens the inferior palpebrae met in a median notch or the lid was divided into halves, which met at an orally directed angle in the middle line.[13] A common caruncula within the notch between the lower lids, such as is seen in the present specimen, has been described in several other cyclopeans but is not of common occurrence.[14] In 2 specimens puncta lacrimalia were present.[15] The presence of two lower lids notched in the median line but with a single caruncula indicates median fusion of this part of the maxillary processes, since the lower lids are derived from the maxillary processes[16] and the caruncula takes its origin from the primordium of the internal portion of the lower lid.[17] The caruncula in the present specimen is represented by a single median mass, and since in normal development there is one caruncula for each internal canthus, it would appear that the median fusion is an upward continuation of the fusion of the maxillary processes without intervention of the field formed by the lower border of the frontal process.

Within the widely open palpebral fissure can be seen the external surface of what appears to be a single eyeball supported in a single orbit. There is a distinct transparent cornea, which is circular in outline. Within this can be seen the outline of an iris, in the middle of which is a definite circular pupil. The bright appearance of the pupil in the photograph would imply that there is an opaque membrane behind this region; otherwise the pigment of the interior would give the pupil a dark color.

The anatomy of the eyeball in human cyclopeans has been examined by many investigators, and all degrees of separation, from a single optic globe to double globes lying within a common orbit, have been described. Thus of 29 reports examined the eyeball was described as single in 13.[18] In 2 specimens the eyeball looked single from the outside, but the globes were separate internally.[10l, m] There was complete duplication in a single orbit with a common palpebral fissure in 10 specimens.[19] There were 4 instances of arrest in development of the optic globe such that the region of the eye was represented by a rudimentary sac.[20] These conditions represent the typical malformations of the eyeball in cyclopia that can be seen in general from the outside. The specimen described here apparently belongs in the class with a single undivided eyeball in a single orbit, although a categorical assertion that this is true cannot be made because necropsy

strosities, Am. J. M. Sc. **84**:129 (July) 1882. (*j*) Falk, J. C.: A Specimen of Cyclocephalus, Philadelphia M. J. **4**:671 (Oct. 7) 1899. (*k*) Wilder, H. H.: The Morphology of Cosmobia, Am. J. Anat. **8**:355 (Dec.) 1908. (*l*) Jackson, H.: Cyclopean Monster, J. A. M. A. **53**:1483 (Oct. 30) 1909. (*m*) Humphrey, R. R.: A Case of Cyclopia in Homo, Anat. Rec. **28**:207 (Aug.) 1924. (*n*) Wilber, I. E.: Human Cyclopia Associated with Other Ocular Anomalies, Am. J. Ophth. **22**:1120 (Oct.) 1939.

11. (*a*) Chapman,[6b] cases 1 and 2. (*b*) Allen.[8c] (*c*) Breckwoldt.[8g] (*d*) Jackson, H.: Cyclopean Monster, Tr. Chicago Path. Soc. **9**:71, 1913. (*e*) Der Brucke, M. G.: Cyclopia, Arch. Ophth. **15**:114 (Jan.) 1936. (*f*) Kuperstein, D.: Cyclops: Case, Am. J. Surg. **33**: 148 (July) 1936. (*g*) De, M. N., and Dutta, H. K.: A Case of Foetus with One Eye (Cyclops), J. Anat. **73**:499 (April) 1939.

12. (*a*) Galloupe, I. F.: Combination of Cyclopia and Anterior Hydrencephalocoele, Boston M. & S. J. **102**: 495 (May 20) 1880. (*b*) Durlacher: Zur Kasuistik der Zyclopie mit Rüsselbildung, Deutsche med. Wchnschr. **41**:1128 (Sept. 16) 1915.

13. (*a*) Ognew.[5] (*b*) Chapman,[6b] cases 1 and 2. (*c*) Allan.[7a] (*d*) Smith and Boulgakow.[7c] (*e*) Allen.[8c] (*f*) Dougal and Bride.[8d] (*g*) Best.[8e] (*h*) Hagens.[8f] (*i*) Breckwoldt.[8g] (*j*) Scott.[10h] (*k*) Koogler.[10i] (*l*) Falk.[10j] (*m*) Wilder.[10k] (*n*) Jackson.[10l] (*o*) Humphrey.[10m] (*p*) Wilber.[10n] (*q*) Francis, D. J. T.: A Short Account of a One-Eyed Monster, London M. Gaz. **34**:580 (Aug.) 1844. (*r*) Jackson.[11d] (*s*) Der Brucke.[11e] (*t*) Kuperstein.[11f] (*u*) De and Dutta.[11g]

14. Smith and Boulgakow.[7c] Allen.[8c] Falk.[10j] Wilder.[10k] Humphrey.[10m]

15. Dougal and Bride.[8d] Wilder.[10k]

16. Kollman, J.: Entwicklungsgeschichte des Menschen, ed. 1, Jena. G. Fischer, 1898.

17. Ask, F.: Ueber die Entwicklung der Caruncula lacrimalis beim Menschen, Anat. Anz. **30**:197 (March) 1907.

18. Burns.[6a] Allan.[7a] Smith and Boulgakow.[7c] Allen.[8c] Breckwoldt.[8g] Scott.[10h] Koogler.[10i] Falk.[10j] Francis.[13q] Der Brucke.[11e] Kuperstein.[11f] De and Dutta.[11g] Bingham, A. W.: Full Term Cyclops, Am. J. Obst. **77**:150 (Feb.) 1918.

19. (*a*) Ognew.[5] (*b*) Chapman,[6b] cases 1 and 2. (*c*) Dougal and Bride.[8d] (*d*) Best.[8e] (*e*) Hagens.[8f] (*f*) Wilder.[10k] (*g*) Wilber.[10n] (*h*) Jackson.[11d] (*i*) von Monakow, C.: Cyklopie mit Verdopplung des Rückenmarken, Wien. med. Wchnschr. **46**:2222 (Dec. 12) 1896.

20. (*a*) Hall.[7b] (*b*) Galloupe.[12a] (*c*) Durlacher.[12b] (*d*) Rothschild, P.: Arhinencephalia completa: Eine neue Form der Achinencephalie mit Betrachtung über die formale und kausale Genese von Ahrinencephalie und Cyklopie, Beitr. z. path. Anat. u. z. allg. Path. **73**:65 (Jan.) 1924.

was not permitted. The underlying causes of these variations will be considered.

A nose is absent. There is no trace of any organ which could resemble a nose. It is well known that when cyclopia occurs in man there is usually a cylindric or piriform proboscis above the single median eye. This may be a simple saclike organ, or in its walls there may be cartilage or even osseous tissue. It is usually pierced at the distal end by a small opening. In 19 of 29 cases which may be taken as representative of conditions of nasal development which have been found in human cyclopean monsters, a proboscis lying immediately above the eye was described. In 16 of these in which the length of the proboscis was given the range was from 10 to 37 mm. (average, 23 mm.); in 13 cases in which the diameter was given the range was from 8 to 20 mm. (average, 13 mm.). Thus it would seem that when an effort at formation of a nose is aborted by the failure of the primordia of the eye to divide there is a degree of regulation of form in the product of this attempt; otherwise the range in size, shape and position of the abortive structure would be considerably greater.

In 1 specimen there was a proboscis below the single eye [7a] but a mouth was lacking, and the condition suggests that this was an abortive attempt to form a mouth from reduced maxillary processes and that it cannot be interpreted as an aborted nose.

In 8 cyclopeans there was no trace of a nose; in 4 which were similar to the specimen here described there was nothing on the forehead above the eye.[21] In 2 specimens the forehead was obliterated by a fluid-filled meningocele.[22] In 1 there was a puffy swelling above the eye;[10h] and in another there was a cartilaginous rudiment above the eye.[19l]

Accordingly, the condition here described is an example of a rare type of arhinencephalia completa accompanying cyclopia completa in which the primordia of the nasal organ have been completely suppressed or have failed to be induced during development. The picture of the present specimen shows this condition to better advantage than any other published pictures.

Below the eye in the normal place for the nose there is a wide stretch of skin where the cheeks are continuous with each other. Such a wide space was present in 18 of 29 specimens whose faces have been described. On the upper margin of this region and just below the eye there is a furrow which marks the lower border of a slight swelling. This line is interpreted to be the result of the fusion of the two suborbital furrows, which in the normal binocular condition are present below the eyes.[23] This feature is present and well marked in 5 of the 29 cyclopeans.[24] Below this furrow and separated from it by a narrow isthmus of skin is a deeper groove extending across the face. This groove is interpreted as having been formed by the confluence of the nasolabial furrows, which in the normal fetus extend from the margins of the nose to the lateral borders of the lips and which in the absence of the nose and by the medial fusion of the maxillary processes extend across the face. This feature was present in the same region in 3 specimens.[25] The space between the two furrows is interpreted as an external expression of a medial fusion of the buccal fat pads. Below the nasolabial groove the upper lip begins to protrude, and this protrusion extends down to the margin of the upper lip. The swelling fades laterally into the regions of the cheeks.

The mouth in the present specimen is complete, but the upper lip lacks a philtrum and a labial tubercle. Such a condition is characteristic of the mouth in human cyclopeans. The philtrum and the labial tubercle are lacking because the median nasal processes were never formed. There is no trace of the fusion which must have taken place between the maxillary processes to complete the upper border of the mouth. Close examination of the mouth shows that there is a large central process which extends downward from the upper lip and meets the broad shelflike lower lip. The lower lip projects in normal fashion and is separated from the chin by the usual sublabial furrow. This condition was present in 17 specimens out of 25 described. In contrast, there were 2 specimens, both synotic, in which the mouth was absent and the ears were in the region of the lateral margins of the chin.[26] A median cleft lip, in which the medial margins of the maxillary processes had failed to fuse, was present in 3 specimens.[27] In 2 specimens the mouth was a rudimentary sac with no

21. Smith and Boulgakow.[7c] Hagens.[8f] Breckwoldt.[8g] Humphrey.[10m]

22. Francis.[13q] Galloupe.[12a]

23. Smith, R. M., and Parker, A. J.: Dissection of a Human Otocephalic Cyclops Monstrosity, Am. J. M. Sc. **84**:132 (July) 1882.

24. Smith.[7c] Dougal and Bride.[8d] Wilder.[10k] Der Brucke.[11e] De and Dutta.[11g]

25. Dougal and Bride.[8d] Der Brucke.[11e] De and Dutta.[11g]

26. Allan.[7a] Francis.[13q]

27. Hagens.[8f] Scott.[10h] Rothschild.[20d]

inferior maxillary region.[28] Microstomia was present in 1 cyclopean.[8g]

From the summary just given of the varying conditions of the mouth in human cyclopeans it can be seen that all degrees of development of the maxillary processes of the first branchial arch occur. These variations also indicate that formation of the upper lip without the median nasal processes is possible and that the maxillary processes have potential powers of growth which are usually limited by the presence of the median and lateral nasal processes. Defective development is an indication of an inherent condition of weakness of the primordia or is the result of the action of external agents on the fundamental primordia at the time when form should be regulated,[29] but the extent of weakness or of biologic deficiency is variable. Thus, in those cases of cyclopia in which the upper lip is not cleft there is relatively little deficiency in the capacity of the parts below the eye to develop along normal lines, but when the lip is cleft or the mouth deficient there is evidence of a greater degree of developmental weakness. Since the molding of these parts is in large measure determined by regulation of the mesoderm,[30] the modern conception is that defective distribution or faulty migration of mesoderm explains not only the failure of the primordia of the eye to divide as they should but also the defective molding of other features of the face.

The auricles of the external ears in this specimen are far down on the sides of the head, and the lower border of the left ear rests on the shoulder. In both ears the dorsal part of the helix, the part contributed by the tissue immediately above the first branchial arch, is lacking. Also, the cephalic part, contributed by the cephalic margins of the cleft, are thicker than normal, giving the ear a "cauliflower" appearance. Malformation of the ears is an unusual accompaniment of cyclopia. Of 28 cyclopeans whose ears were mentioned there was none in whom both ears were absent. In 1 specimen the left ear was absent and the right was normal,[8f] and in 1 the external ears were underdeveloped.[11d] There were 2 specimens with synotica.[31] In 1 specimen the ears were well down on the neck and were larger than normal.[7b] In only 1 [20d] cyclopean were the parts deficient in the same regions and folded in the same manner as in the specimen described here. In 1 specimen the ears were abnormally large.[10m] In the remaining 21 there was nothing unusual about the external ears.

EARLY EMBRYONIC RELATIONS OF OPTIC PRIMORDIA

To attempt an explanation of the factors in early human development which underlie the production of cyclopia, one must understand the relations of those parts of the embryo which precede the actual morphologic appearance of the optic primordia. The earliest appearance of the optic primordia which can be morphologically identified was stated by Bartelmez and Evans [32] to be present in a young human embryo of 8 somites (H87, University of Chicago collection). These primordia are two grooves, the optic sulci, which, arising in the laterodorsal part of the primordium of the forebrain, extend obliquely mesiad and terminate in a thickened medial plate which is unpaired, the so-called torus opticus. Prior to this time the neural plate, such as is present in the Ingalls embryo of 2 somites,[33] shows the primordium of the plate of the forebrain with a suggestion of the optic sulci. The crucial stage at which cyclopia may be initiated must occur before this stage of development. This conception is held by those investigators who have examined by experimental methods the morphologic conditions incident to the production of cyclopia in amphibia. These experiments were reviewed in detail by Adelmann,[34] and an analysis of the data indicated that chemical and physical agents acting on embryos prior to the appearance of the primordia of the eye cause cyclopia. Also, experiments in extirpation and transplantation have shown that the whole region of the forebrain prior to the appearance of bilateral optic primordia is capable of forming eyes from any region, but that the formation is best from median pieces. Hence the idea has arisen that the optic primordia are gradually localized laterally under the influence of some agent of induction which modifies the primitive general potency for production of the eyes. The part which Adelmann [30] considered to be the causa-

28. (*a*) Smith and Boulgakow.[7c] (*b*) Koogler.[10l] The same case is described by Smith and Parker.[23]

29. Holtfreter, J.: Formative Reize in der Embryonalentwicklung der Amphibien, dargestellt an Explanationsversuchen, Arch. f. exper. Zellforsch. **15**:281, 1934; cited by Adelmann.[34]

30. Adelmann, H. B.: A Study of Cyclopia in Amblystoma Punctatum with Special Reference to the Mesoderm, J. Exper. Zoöl. **67**:217 (Feb.) 1934.

31. Koogler.[28b] Francis.[13q]

32. Bartelmez, G. W., and Evans, H. M.: Development of the Human Embryo During the Period of Somite Formation, Including Embryos with 2 to 16 Pairs of Somites, Contrib. Embryol. **17**:1 (Feb.) 1926.

33. Ingalls, N. W.: A Human Embryo at the Beginning of Segmentation with Special Reference to the Vascular System, Contrib. Embryol. **11**:61 (Jan.) 1920.

34. Adelmann, H. B.: The Problem of Cyclopia: I., Quart. Rev. Biol. **2**:161 (June) 1936; II., ibid. **2**:284 (Sept.) 1936.

tive agent in this bilateral induction is the prechordal plate, a mass of tissue (mesentoderm) lying in the roof of the most cephalic part of the archenteron at the stage immediately preceding the appearance of bilateral optic primordia. In experimental procedures in which cyclopia has occurred after the exposure of amphibian embryos to lithium salts, the prechordal plate, which normally flattens and progresses laterally, does not do so. Whether this relation between failure of the prechordal plate to produce bilateral formation of the eyes is mechanical or chemical has not been decided.

Similar conditions of development in human embryos before the morphologic appearance of primordia of the eye can be found in the McIntyre embryo,[35] in which there was a rather extensive prochordal plate (the morphologic antecedent of the prechordal plate) underlying the cephalic part of the early neural plate. And in the embryos of still younger stages described by Heuser [36] and George[37] the prochordal plate lay in the roof of the archenteron but no neural plate was present as yet in this part of the embryonic disk. Hence if inhibition of or interference with the growth of the neural plate to form bilateral primordia of the eyes is to occur it must take place between the stages represented by the embryos of Heuser and George and the stage described by Ingalls or that of Bartelmez and Evans.

Unfortunately the interval of time between these stages in human embryos is not definitely known. Time seems to me an important factor to consider if information gained from experiments with animals is to be applied to human development. Not only are human beings different from animals in certain morphologic and physical aspects, but the time relation of the changes in their tissues to their environment is different. In the preceding paragraph it was pointed out that the morphologic conditions preceding development of the eye in human beings are similar in a general way to those in amphibia, but the element of time is different. We know from the measurements of these periods in the lower vertebrates that a certain interval of time elapses between the first appearance of the neural plate and the morphologic appearance of the primordia of the eye. I have estimated this interval as follows from the data in published tables of early development in certain vertebrates: in the embryo of the frog, for Rana sylvatica four hours[38] and for Rana pipiens twelve hours[39]; in the embryo of the salamander for Triturus pyrrhogaster twelve hours [40] and for Amblystoma punctatum six hours [41]; in the embryo of the chick four hours [42]; in the embryo of the guinea pig twenty-four hours [43]; in the embryo of the rabbit seven hours,[44] and in that of the macaque monkey two days.[45] Examination of these data shows that the greatest interval of time between these two stages occurs in the growth of the monkey embryo. If it is assumed that there is little difference between monkeys and human beings as regards the time of appearance of certain structures it may be concluded that these changes occur in human beings between the nineteenth and twenty-first day of development. Hence if certain environmental conditions can affect the neural plate so that the formation of bilateral primordia of the eye is inhibited the time during which these detrimental influences may act is considerably longer in human beings than in the lower vertebrates. The failure of the neural plate to undergo proper morphologic changes also involves changes which could affect the bilaterality of the whole cephalic end of the head, including the forehead, the nasal organs and the brain.[34] The degrees of cyclopia which are accompanied by varied morphology of other parts of the head can therefore be related to time as well as to early morphologic relations. In the present specimen the modifications have affected the eye, the forehead and the nasal primordia, but no information is available concerning the brain, although from the descriptions of cyclopeans referred to in the preceding pages it would appear that the cerebral part of the brain is usually deficient.

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37. George, W. C.: A Presomite Human Embryo with Chorda Canal and Prochordal Plate, Contrib. Embryol. **30**:1 (Dec.) 1942.

38. Pollister, A. W., and Moore, J. A.: Tables for the Normal Development of Rana Sylvatica, Anat. Rec. **68**:489 (July) 1937.

39. Shumway, W.: Stages in the Normal Development of Rana Pipiens, Anat. Rec. **78**:139 (Oct.) 1940.

40. Anderson, P. L.: The Normal Development of Triturus Pyrrhogaster, Anat. Rec. **86**:1 (May) 1943.

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42. Duval, M.: Atlas d'embryologie, Paris, G. Masson, 1889.

43. Scott, J. P.: The Embryology of the Guinea Pig, Am. J. Anat. **60**:397 (March) 1937.

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DEVELOPMENT OF GALACTOSE CATARACT IN THE ALBINO RAT EMBRYO

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In 1935 Mitchell [1] first reported the type of cataract in rats which results from a diet containing a high level of galactose. Subsequent investigation [2] brought out the fact that galactose cataract occurred more readily in younger than in older animals, and consequently it became of interest to determine the effect of galactose on the developing lens of the rat embryo. A series of investigations, begun in 1937, have definitely established the fact that when pregnant female rats are fed a diet containing 25 per cent galactose cataractous changes appear in the lenses of the embryos.[3]

Because of variations in the degree of susceptibility of different strains of rats,[4] the investigation included animals from the original Battle Creek stock, known to be highly susceptible, and from a closely inbred strain which had been used in the Wellesley College laboratory for several years. Preliminary experiments with a lactose diet established the latter strain as somewhat less susceptible. In addition, a hybrid strain was developed by mating males of the Battle Creek strain with females of the Wellesley College strain. Any study of rat embryos brings out the fact that not only do litters vary but individuals within the same litter may show a wide divergence in the stage of development reached within a given time. General conclusions as to the condition at a particular age must be based on a study of a considerable number of individual embryos. Moreover, a knowledge of normal development is essential to the interpretation of abnormal conditions. Therefore, with the three strains of rats, a careful study has been made of more than 300 lenses from a normal series and an approximately equal number from the experimental series.

All of the control animals and all of the females up to the onset of pregnancy were fed a standard ration consisting of Purina dog chow (obtained from the Purina Mills, St. Louis) and lettuce. The original experimental diet was modified according to suggestions made by Dr. Mitchell and was designed to satisfy the increased requirements of pregnancy.[5] Determination of the age of the embryos was based on the calculations of Long and Evans,[6] who asserted that fertilization of the eggs might occur at any time within twenty-four hours after copulation. Accordingly, the second day after the appearance of sperm in the vaginal smear was regarded as the first day of gestation, and the rats were 21 days old at the time of birth.

The lens is a particularly difficult organ to prepare for histologic investigation, and it was necessary to try several methods before satisfactory sections could be secured.[7] The procedure which ultimately gave the greatest detail

1. Mitchell, H. S.: Cataract in Rats Fed on Galactose, Proc. Soc. Exper. Biol. & Med. **32**:971, 1935.

2. Mitchell, H. S., and Cook, G. M.: Galactose Cataract in Rats, Arch. Ophth. **19**:22 (Jan.) 1938.

3. Bannon, S. L., and Kaan, H. W.: Normal Development of the Lens in the Albino Rat and the Effect of a Diet High in Galactose, Anat. Rec. (supp.) **73**:59, 1939. Mandrey, J. L.: Development of Cataract in the Embryonic Lens of the Albino Rat, ibid. (supp.) **76**:92, 1940. MacRae, R.: Cataractous Lenses of the Albino Rat, Stained for Presence of Fat, ibid. (supp.) **79**:74, 1941.

4. Mitchell, H. S.: Susceptibility of Different Strains of Rats to Nutritional Cataract, J. Nutrition **12**:447, 1936.

5. The composition of the experimental ration was as follows:

Corn starch	40%
Galactose	25%
Casein	15%
Hydrogenated cotton seed oil (Crisco)	9%
Wheat germ	5%
F.R.L. salt mixture*	4%
Cod liver oil	2%
Brewers' yeast (given 6 days a week)	0.5 Gm.

* Substituted for the Osborne-Mendel salt mxiture (F. R. L. salt mixture is described in Hawk, P. B., and Bergeim, O.: Practical Physiological Chemistry, ed. 11, Philadelphia, P. Blakiston's Son & Co., 1942, p. 887).

6. Long, J. A., and Evans, H. M.: The Oestrus Cycle in the Rat and Its Associated Phenomena, Mem. Univ. California **6**:17, 1922.

7. Dr. Theodore L. Terry, of the Massachusetts Eye and Ear Infirmary, Boston, gave assistance and suggestions in the initial stages of the investigation.

of cell structure with the least possible shrinkage and distortion of tissues consisted in preservation in Perényi's fluid, dehydration in alcohol, clearing in cedar oil and embedding in paraffin. It proved difficult to remove the lens without injury and consequent disturbance of the histologic picture. Better results were secured when the lens remained within the eye. However, serial sections were made of both lenses and eyes. These were cut at 10 microns and stained with Delafield's hematoxylin and eosin.

Normal development of the lens showed considerable similarity in all three strains of rats, and the early stages resembled closely the same stages in the rabbit, as described by Rabl.[8] With increasing differentiation of the lens there appeared greater variation between individual rats, and even between the two eyes of the same animal. Development evidently did not progress uniformly throughout the lens. Certain conditions could be considered characteristic of each age, however.

The placode of the lens appeared as a thickening of ectoderm at the age of 10 days. Invagination and closure of the lens vesicle occurred during the eleventh day, and the vesicle became separated from the overlying ectoderm on the twelfth day. At this time cells in the posterior portion had begun to lengthen; and by the thirteenth day the lumen of the vesicle was almost obliterated by growth of the posterior cells, and there was an obvious distinction between the anterior epithelium and the posterior fibers of the lens. By the fourteenth day the anterior epithelium consisted of a single layer of high cuboidal cells, which became columnar at the equator. Growth of the posterior fibers had been greater in the central region, with consequent forward migration of their nuclei. Sections through the dorsoventral axis at this stage showed the nuclei in a curve following the curve of the anterior surface of the lens. A few lenses at the 14 day stage showed extremely small, single vacuoles either within or between certain of the posterior fibers. These vacuoles were apparently empty and were not numerous. In the 15 day lens the most conspicuous feature was the great increase in vacuoles. They had spread throughout the entire central portion and occupied a region which was roughly V shaped in section, with the angle of the V at the posterior pole of the lens and the broad area immediately below the anterior epithelium. The vacuoles might occur singly or in groups, and certain of them contained a fine reticulum, which stained pink with eosin. They decreased rapidly in number during the sixteenth day. Those that remained appeared, generally, at the posterior pole of the lens in the region where the fibers were converging to form the posterior suture (fig. 1 *A*). This suture showed distinctly at 17 days as a depression in the posterior pole of the lens at the point where the hyaloid artery touched the capsule (fig. 1 *B*). In section, the suture was in the form of an inverted V and contained dark-staining granular material, in which were a few vacuoles of varying sizes.

Further differentiation of the lens occurred at 18 days. The anterior epithelium became low cuboidal. The central fibers developed into the nucleus of the lens, a change which involved enlargement of the individual fibers and gradual disappearance of their nuclei. The structure of the cytoplasm altered, some fibers staining more and others less deeply (fig. 1 *C*) but all being densely granular. Fibers just peripheral to the lens nucleus showed a fine reticular cytoplasm and appeared pale, in contrast to the fibers of the nucleus itself. All fibers immediately outside the lens nucleus converged toward the posterior suture, which frequently contained more or less dark-staining granular material and vacuoles. By this time vacuoles had entirely disappeared from the main body of the lens. At the anterior pole a few peripheral fibers met above the lens nucleus to form the anterior suture. At 19 and 20 days both the sutures and the lens nucleus became increasingly distinct, as a result of continued growth of the lens. In lenses of the hybrid and Battle Creek strains, closure of the posterior suture was definitely delayed; granular material continued to accumulate in the suture, and one or more large vacuoles were present at its inner tip. In the lens of the full term rat (fig. 1 *D*), the anterior epithelium was low. The lens nucleus had increased in size through incorporation of the surrounding fibers. The anterior suture was more distinct. The posterior suture was almost or completely closed. In some cases, it still contained small vacuoles throughout its length or at its inner tip, and in certain lenses a band of small vacuoles extended outward from the suture across the posterior part of the lens.

Lenses from the experimental animals showed no striking deviation from normal through the fifteenth day of gestation. At 16 days, however, cataractous changes began to appear. Again, as in the normal series, individual differences were evident. Some of these could be explained on the basis of differences in the degree of sus-

8. Rabl, C.: Ueber den Bau und die Entwicklung der Linse, Ztschr. f. wissensch. Zool. **67:1**, 1900.

ceptibility to the cataractogenic diet. For instance, two entire litters of 18 day fetuses, one from the Wellesley and one from the hybrid strain, showed no obvious variation from normal.

In the initial stage, at 16 days (fig. 2 *A*), the entire central portion of the lens was completely vacuolated. Increase in the number of vacuoles and coalescence of some to form large, irregular

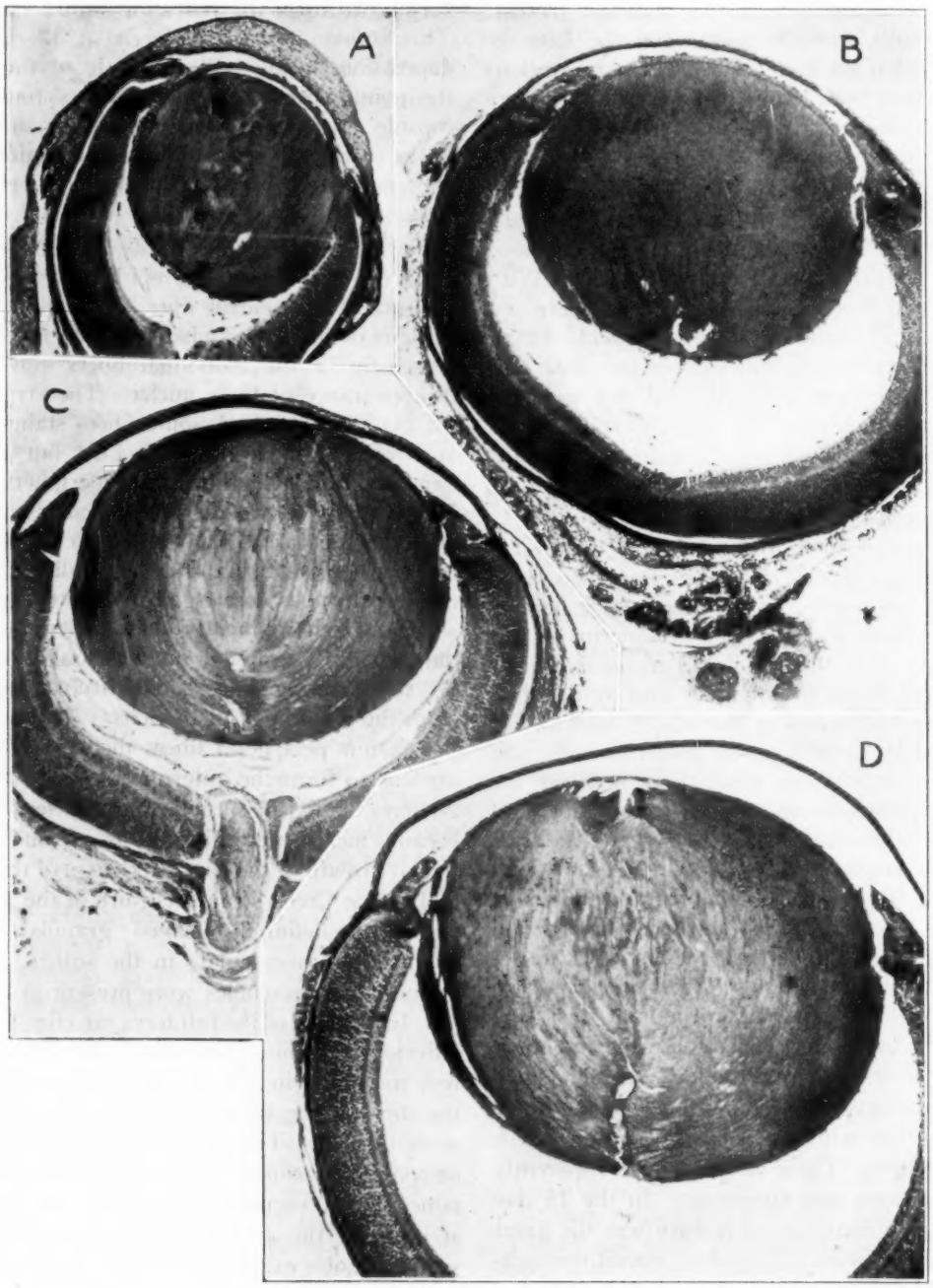

Fig. 1 (normal series).—*A*, eye of a 16 day embryo; hybrid strain. *B*, eye of an 18 day fetus; Wellesley College strain. *C*, eye of an 18 day fetus; Wellesley College strain. *D*, eye of a full term rat; Wellesley College strain.

In all the other animals, however, the lenses appeared distinctly abnormal, and the cataractous changes were generally most severe in the Battle Creek strain.

spaces characterized the condition at 17 days (fig. 2 *C*). Closure of the posterior suture was slow and permitted greater accumulation of granular material at the posterior pole (fig. 2 *B*).

After extensive vacuolation, fibers of the lens nucleus began to lose their structure and were replaced by masses of dense granular material. The degenerative changes appeared first at the anterior pole of the lens nucleus (fig. 2 *D*); large, irregular spaces continued to be present at the posterior pole of the lens nucleus. Other, smaller, vacuoles extended generally throughout the length of the posterior suture. In many cases closure of the suture did not occur, and a wide V-shaped or Y-shaped depression was filled with granular material and vacuoles. Beginning at 19 days, a band of vacuoles spread peripherally across the posterior part of the lens. These vacuoles radiated from the suture (fig. 2 *E*) and appeared in many cases to be located

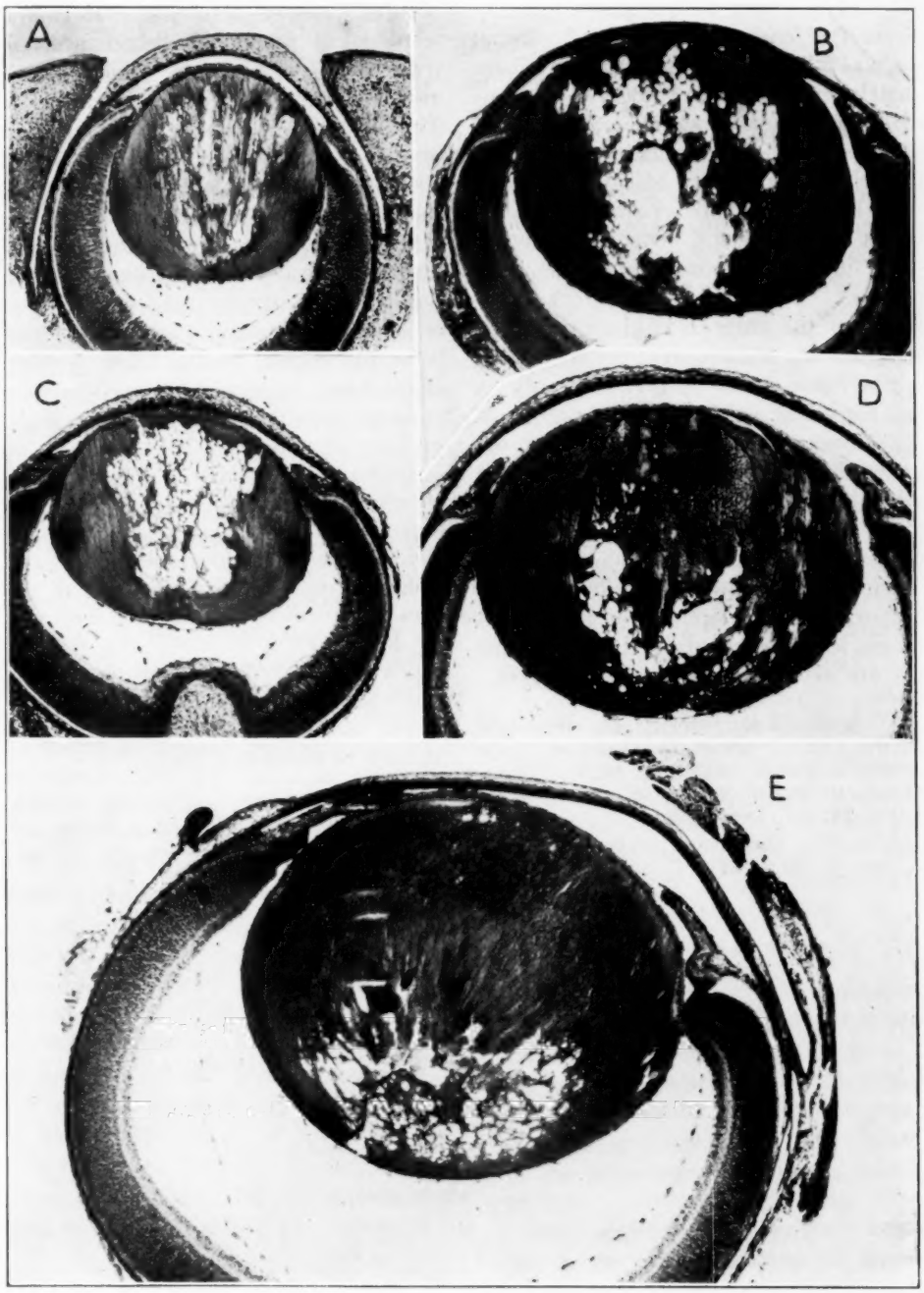

Fig. 2 (cataract series).—*A*, eye of a 16 day embryo; hybrid strain. *B*, eye of an 18 day fetus; Battle Creek strain. *C*, eye of a 17 day fetus; hybrid strain. *D*, eye of a 19 day fetus; Wellesley College strain. *E*, eye of a 20 day fetus; Battle Creek strain.

within the fibers themselves. This band increased in extent and was a conspicuous feature of the full term cataractous lens.

Ophthalmoscopic observations on the embryonic lenses were impossible. The histologic changes, however, could be compared directly with those in the lenses of adult rats.[9] Initial vacuolation was followed by degeneration of fibers and, ultimately, replacement of fibers by a granular mass of noncellular material. Splitting of the suture lines by the accumulation of fluid is also characteristic of this type of cataract.[10] Minute vacuoles beneath the anterior epithelium were observed, but not with sufficient regularity to warrant their inclusion among the specific cataractous changes. There was no apparent modification of either the anterior epithelium or the lens capsule, and any separation of the epithelium from the lens fibers could be regarded only as an artefact, the result of the histologic methods employed. Presence of granular material between the epithelium and the fibers indicated mechanical injury to the lens, inasmuch as it occurred only in lenses which had been removed from the eyes and had suffered distortion or fracture during the operation. While it is evident, therefore, that development of cataract in the embryonic lens is comparable to that in the adult, there are nevertheless obvious differences.

The location of the primary area of degeneration within the lens nucleus is a characteristic of cataract in the young. Yudkin and Arnold[11] found that in young rats the initial opacity occurred in the nucleus, whereas in older rats a cortical cataract developed. If cataract is the result of a metabolic disturbance, presumably those areas of the lens which have a higher metabolic rate should be the most susceptible. The sequence of cataractous changes in the embryo is clearly related to developmental changes within the lens. Onset of the cataract affects the central fibers, which are undergoing modifications preparatory to the formation of the lens nucleus. As development progresses, closure of the posterior suture marks another region of cellular activity, and cataractous changes shift from the central to the more posterior region of the lens. Sections of normal lenses show that vacuoles arise apparently as the accompaniment of normal activity. The extreme vacuolation seems to be due to continuation and exaggeration of a condition which already exists within the lens. Comparison of the photomicrographs, which were all taken at the same magnification, makes it apparent that presence of the cataract does not interfere with normal increase in size of the lens. Thus, it is not the growing regions which are affected but those portions of the lens which are undergoing differentiation.

The photomicrographs were taken by Mr. R. W. St. Clair of Cambridge, Mass.

9. Gifford, S. R., and Bellows, J.: Histologic Changes in the Lens Produced by Galactose, Arch. Ophth. **21**:346 (Feb.) 1939. Dodge, W. M., Jr.: Histopathologic Characteristics of Nutritional Cataract in the White Rat, ibid. **14**:922 (Dec.) 1935.

10. Yudkin, A. M.: Diet and Vitamins in Relation to Cataract, Am. J. Ophth. **21**:871, 1938.

11. Yudkin, A. M., and Arnold, C. H.: Cataracts Produced in Albino Rats on a Ration Containing a High Proportion of Lactose and Galactose, Arch. Ophth. **14**:960 (Dec.) 1935.

FREQUENCY AND LOCATION OF PUNCTATE OPACITIES IN THREE HUNDRED YOUNG CRYSTALLINE LENSES

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The frequency of opacities in the young crystalline lens is so great that it has been considered physiologic by some ophthalmologists. Pellaton,[1] examining 82 children in Basel, Switzerland, found punctiform opacities in 96 per cent of them. Vogt[2] wrote that in a somewhat older group peripheral hooklike opacities were present in 10 per cent, embryonal axial opacities in the region of the anterior embryonal sutures in 20 per cent and various forms of punctate opacities in the region of the posterior Y sutures in 10 per cent. He stated that the number of punctate opacities increases with age and in the fifth and sixth decade hardly a lens is free of such opacities. This statement recalls the famous dictum of Walther[3] that every one who does not die prematurely becomes cataractous.

The purpose of the investigation herein reported was to determine the incidence of opacities in Americans between 18 and 40 years of age and to correlate changes and age in the hope that light might be thrown on the causation of senile cataract. The slit lamp examinations, which were conducted in a United States Army general hospital, were made while the eyes were under homatropine cycloplegia. Altogether 150 subjects, or a total of 300 eyes, were examined. Eyes showing signs of ocular disease or of trauma were excluded.

According to the site in the lens in which they were located, the opacities were classified into the following groups:

A. Those between the anterior band of the lens and the posterior surface of the band of disjunction (fig. 1 *A* and table, column A).

B. Those between the posterior surface of the band of disjunction and the region of the anterior Y suture (fig. 1 *A* and table, column B).

C. Those in the region of the anterior Y suture, including that section of the lens lying between the anterior fetal nuclear band and the anterior surface of the central dark interval (fig. 1 *B* and table, column C).

D. Those in the central dark interval itself.

E. Those in the region of the posterior Y suture, including the area from the central dark interval up to and including the posterior fetal nuclear band (fig. 1 *B* and table, column E).

F. Those between the posterior fetal nuclear band and the anterior surface of the posterior band of disjunction (table, column F).

G. Those from (and including) the posterior band of disjunction to the posterior surface of the lens (table, column G).

The eyes were also divided into two groups, those with few opacities (F) and those with numerous opacities (N) (table, column H). Capsular pigmented stars (P. S.) and persistent pupillary strands (P. M.) were noted (table, column I).

OBSERVATIONS

Only 8 of the 300 eyes examined were entirely free of opacities of the lens. All others showed punctate opacities in one or more sections of the lens. Because of the difficulty of differentiating between congenital and presenile forms of punctate opacities, the latter were considered to be physiologic and were included in this survey.

Sixty-eight eyes (23 per cent) contained opacities in the region between the anterior band of the lens and the posterior surface of the anterior band of disjunction. Somewhat deeper in the lens (between the band of disjunction and the region of the anterior Y suture) opacities were much more numerous, being present in 227 eyes (76 per cent). In the central portions of the lens the opacities diminished in number (44 eyes,

1. Pellaton, R.: Die physiologischen Linsentrübungen im Kindesalter nach Spaltlampenuntersuchung an 164 normalen Kinderaugen, Arch. f. Ophth. **111**:341-351, 1923.

2. Vogt, A.: Lehrbuch und Atlas der Spaltlampenmikroskopie des lebenden Auges, Berlin, Julius Springer, 1930-1931.

3. Walther, cited by Norris, W. F., and Oliver, C. A.: A Textbook of Ophthalmology, Philadelphia, Lea Bros. & Co., 1893.

Patient	Age, Yr.	Sex	Eye	A*	B	C	D	E	F	G	H	I	Comment
1	25	♂	1	..	+	..	..	..	+	..	N	.....	Bilateral coronary and cerulean cataracts
			2	..	+	..	..	..	+	..	N	.....	Bilateral coronary and cerulean cataracts
2	18	♂	3	..	..	..	+	+	..	..	F	.....	
			4	..	..	..	..	..	..	..	..	.....	Clear
3	28	♂	5	..	−	..	..	..	..	..	F	.....	
			6	..	..	..	..	..	..	..	..	.....	Clear
4	36	♂	7	..	+	+	..	+	+	..	N	.....	
			8	+	+	+	..	+	+	+	N	.....	Opacities most numerous nasally
5	35	♂	9	..	+	..	+	..	+	..	F	.....	Nuclear relief
			10	..	+	+	..	+	+	..	F	.....	Nuclear relief
6	21	♂	11	+	..	..	+	..	..	..	F	.....	Opacities situated nasally
			12	..	+	..	..	..	+	..	F	.....	Opacities situated nasally
7	37	♂	13	..	+	..	..	..	+	..	N	.....	Nuclear relief marked; opacities most
			14	..	+	..	..	..	+	..	N	.....	numerous nasally in both lenses
8	27	♂	15	..	+	..	..	..	+	+	N	.....	
			16	..	+	..	..	+	+	+	N	.....	
9	20	♂	17	+	..	..	..	+	..	..	F	.....	
			18	..	+	..	+	..	..	+	F	.....	
10	30	♂	19	..	+	..	..	..	..	..	F	.....	
			20	..	..	+	..	..	..	..	F	.....	
11	25	♂	21	..	..	..	..	..	..	..	..	.....	Lens clear
			22	..	..	..	..	..	..	..	..	.....	Lens clear
12	18	♂	23	..	..	..	..	..	..	..	..	.....	Lens clear
			24	..	..	..	..	..	..	..	..	.....	Lens clear
13	30	♂	25	..	+	..	..	..	+	..	N	.....	Coronary cataract
			26	..	+	..	..	..	+	..	N	.....	Coronary cataract
14	18	♂	27	+	+	..	..	..	+	+	F	.....	
			28	+	+	+	..	..	+	+	H	.....	
15	19	♂	29	+	..	..	..	..	..	+	F	.....	Few streaks in periphery also present
			30	+	..	..	..	..	..	+	F	.....	Few streaks in periphery also present
16	20	♂	31	..	+	..	..	..	..	..	F	.....	Single punctate and linear opacities in
			32	..	+	..	..	..	..	..	F	.....	lower nasal quadrants
17	38	♂	33	..	+	..	..	..	..	..	F	.....	
			34	..	+	..	..	..	..	..	F	.....	Punctate opacities situated nasally
18	20	♂	35	..	+	..	..	..	..	..	F	.....	Opacities situated entirely nasally
			36	..	−	..	..	..	..	..	F	P. S.	Opacities situated entirely nasally
19	21	♂	37	..	..	+	..	..	+	..	F	.....	
			38	..	+	..	..	..	..	..	F	.....	Single dot on temporal side
20	38	♂	39	..	+	+	..	+	+	..	N	.....	Bilateral triradiate and coronary cataracts
			40	..	+	+	..	+	+	..	N	.....	Bilateral triradiate and coronary cataracts
21	24	♂	41	+	+	+	..	..	+	+	F	.....	
			42	+	+	+	..	..	+	+	F	.....	
22	33	♂	43	+	+	..	..	..	+	+	F	.....	Opacities situated in periphery, particularly
			44	+	+	..	..	..	+	+	N	.....	nasally
23	36	♂	45	..	..	..	..	..	..	..	..	P. S.	Lens clear
			46	+	+	..	..	..	+	+	F	.....	
24	28	♀	47	+	+	..	..	..	+	+	F	.....	Bilateral punctate opacities on the anterior
			48	+	+	..	..	..	+	+	F	.....	cortical suture system
25	24	♂	49	..	+	..	..	..	+	..	F	P. M.	
			50	..	+	..	..	..	+	..	F	.....	
26	27	♂	51	..	+	..	..	..	..	..	F	P. M.	Opacities situated mainly nasally
			52	..	+	..	..	..	..	..	F	.....	Opacities situated mainly nasally
27	22	♂	53	+	+	..	..	..	..	..	F	P. M.	
			54	+	+	..	..	..	..	..	F	.....	Opacities situated mainly nasally
28	24	♂	55	..	+	..	..	..	+	..	F	.....	Opacities situated mainly nasally
			56	..	+	..	..	..	+	..	F	.....	Opacities situated mainly nasally
29	35	♂	57	+	..	..	..	..	..	..	N	.....	
			58	+	..	..	..	..	..	..	N	P. S.	
30	26	♂	59	+	..	..	..	..	+	..	F	P. M.	
			60	..	..	..	..	..	..	..	..	P. M.	Lens clear
31	27	♂	61	+	+	..	..	..	+	+	F	.....	
			62	+	+	..	..	..	+	+	F	.....	Opacities in periphery
32	22	♂	63	..	..	..	..	+	..	..	F	P. S.	
			64	..	..	..	..	+	..	..	F	.....	
33	25	♂	65	..	+	+	..	..	..	..	F	P. S.	
			66	..	+	..	..	..	..	..	F	.....	Cataracta cerulea
34	37	♂	67	+	+	..	..	..	..	..	F	.....	Opacities situated entirely nasally
			68	+	+	..	..	..	..	..	F	.....	Opacities situated entirely nasally
35	31	♂	69	..	+	..	..	+	+	..	F	P. S.	
			70	..	+	..	..	+	+	..	F	.....	Opacities situated mainly nasally
36	19	♂	71	..	..	..	+	..	..	..	F	.....	
			72	+	+	..	..	..	..	..	F	.....	Several faint whitish linear opacities on anterior capsule
37	27	♂	73	..	+	..	..	..	+	..	N	.....	Retrofridial pigmented striae on anterior
			74	..	+	..	..	..	+	..	N	.....	lens surface of both eyes
38	27	♂	75	+	+	..	..	..	+	+	N	.....	
			76	+	+	..	..	..	+	+	N	.....	Anterior rosette-shaped cataract (nontraumatic)

* See text for interpretation of symbols.

Patient	Age, Yr.	Sex	Eye	A*	B	C	D	E	F	G	H	I	Comment
39	30	♂	77	+	+	..	..	..	+	..	F	.....	
			78	+	+	..	..	..	+	..	F	.....	
40	22	♂	79	..	..	..	..	..	+	..	F	.....	
			80	..	..	..	..	+	+	..	F	.....	
41	36	♂	81	+	+	+	..	+	+	+	N	.....	Opacities situated mainly nasally
			82	+	+	..	..	..	+	+	N	.....	Opacities situated mainly nasally
42	18	♂	83	..	..	..	+	..	..	..	F	.....	
			84	..	+	..	..	..	..	..	F	.....	
43	19	♂	85	..	+	..	+	..	..	..	F	P. S.	
			86	..	..	..	+	..	..	..	F	P. S.	
44	22	♂	87	..	+	..	+	..	+	..	F	.....	
			88	..	+	..	+	..	+	..	N	.....	
45	27	♂	89	..	+	+	+	..	..	..	F	.....	
			90	..	..	..	+	..	+	..	F	P. S.	
46	23	♂	91	..	..	+	+	..	..	..	F	.....	Opacities situated inferiorly
			92	..	+	+	..	..	+	..	F	.....	Opacities situated mainly nasally
47	27	♂	93	..	+	..	..	..	+	..	N	.....	Opacities in both lenses more numerous
			94	..	+	..	..	..	+	..	N	.....	posteriorly and inferiorly
48	21	♂	95	..	+	+	+	..	+	..	F	.....	
			96	..	..	+	..	+	..	..	F	.....	
49	34	♂	97	..	+	..	+	..	..	..	F	.....	Nuclear relief
			98	..	+	..	+	..	..	..	F	.....	Nuclear relief
50	21	♂	99	..	+	..	+	..	..	+	F	P. M.	Opacities situated mainly nasally
			100	..	+	..	..	..	+	..	F	.....	Opacities situated mainly nesally
51	28	♂	101	..	+	+	..	+	..	..	N	.....	
			102	..	+	..	..	+	+	..	N	.....	
52	34	♂	103	..	+	..	..	+	..	..	F	P. S.	
			104	..	+	+	..	+	+	..	F	P. S.	
53	22	♀	105	+	+	..	+	..	+	+	F	.....	Opacities situated mainly nasally
			106	..	+	..	..	..	+	+	N	.....	Opacities situated mainly nasally
54	23	♀	107	+	..	+	+	+	+	+	F	.....	
			108	+	..	+	..	..	..	+	N	.....	
55	29	♀	109	..	+	..	..	..	+	..	F	.....	Opacities situated mainly nasally
			110	..	+	..	+	+	..	+	F	.....	1 opacity on posterior surface
56	22	♀	111	..	+	+	..	..	+	+	F	.....	Cortical opacities situated mainly nasally
			112	..	+	+	..	..	+	+	F	.....	Cortical opacities situated mainly nasally
57	25	♂	113	..	+	..	+	..	..	+	F	.....	
			114	..	+	..	+	..	..	..	F	.....	
58	23	♂	115	..	+	..	+	..	..	..	F	.....	
			116	+	..	..	+	..	..	..	N	.....	
59	35	♀	117	..	+	..	..	..	..	..	N	.....	Nuclear relief
			118	..	+	..	..	..	+	+	N	.....	Nuclear relief
60	35	♂	119	+	+	..	+	..	+	..	N	.....	Anterior sutural cataract (presenile type)
			120	+	+	..	+	..	+	+	N	.....	and cuneiform opacities; same as 119 except cuneiform opacities absent
61	25	♂	121	..	+	..	..	..	+	..	F	.....	Also shows 1 striate opacity situated nasally
			122	..	+	..	..	..	+	..	F	.....	
62	20	♂	123	..	+	+	..	+	+	..	N	P. S.	Anterior cortical opacities situated nasally
			124	..	+	..	..	..	+	..	N	P. S., P. M.	
63	28	♂	125	+	+	+	..	+	+	..	N	P. M.	One linear opacity present inferiorly
			126	..	+	+	..	+	+	..	N	.....	
64	49	♀	127	+	+	..	+	..	+	+	F	.....	Peripheral concentric lamellar and nuclear
			128	..	+	..	+	..	+	..	F	P. S.	relief present in both eyes
65	34	♂	129	+	+	..	..	+	+	..	F	.....	Wreath of faint lines on anterior lens sur-
			130	..	+	..	..	+	+	..	F	.....	face of each eye
66	24	♂	131	..	+	..	..	..	..	..	F	P. M.	
			132	..	+	+	..	..	+	..	F	P. S.	Opacities situated mainly nasally
67	21	♂	133	+	..	..	..	..	..	..	F	P. M.	Pupillary strand extending from pupillary
			134	..	..	..	..	+	..	..	F	.....	margin to opacity on lens surface
68	33	♂	135	+	..	..	+	..	..	..	F	.....	
			136	..	+	..	+	..	..	..	F	.....	
69	21	♂	137	..	+	..	..	..	+	..	F	.....	Peripheral concentric lamellar opacities
			138	..	+	..	..	+	..	+	F	.....	
70	23	♂	139	..	+	..	..	..	..	+	F	P. M.	
			140	..	+	..	..	+	+	+	F	P. M.	Opacities situated mainly nasally and also inferiorly
71	25	♂	141	..	+	..	..	..	..	..	F	.....	Opacities situated nasally and inferiorly
			142	..	+	..	..	..	+	..	F	.....	Opacities situated nasally and inferiorly
72	23	♂	143	..	+	..	..	..	+	+	N	P. S.	Peripheral concentric lamellar opacities
			144	..	+	..	..	..	+	..	N	P. S.	Peripheral concentric lamellar opacities
73	26	♂	145	..	+	..	+	..	..	..	F	.....	
			146	..	..	+	..	+	+	+	F	.....	
74	22	♂	147	..	..	..	+	..	..	..	F	.....	
			148	+	..	..	..	..	..	..	F	.....	
75	34	♂	149	..	+	+	+	+	+	..	N	.....	
			150	..	+	+	+	+	+	..	N	.....	
76	19	♂	151	..	+	..	..	+	+	..	F	.....	
			152	..	+	..	..	+	+	..	F	P. S.	

* See text for interpretation of symbols.

Patient	Age, Yr.	Sex	Eye	A*	B	C	D	E	F	G	H	I	Comment
77	38	♂	153	+	+	..	+	+	+	..	N	.....	Slight nuclear relief in both eyes
			154	..	+	..	..	..	+	..	N	P. S.	
78	40	♂	155	..	+	..	..	..	+	..	N	.....	Most opacities situated inferiorly and nasally
			156	..	+	+	+	+	+	..	N	.....	
79	21	♂	157	..	..	..	..	+	+	..	F	.....	
			158	+	+	..	..	..	+	..	F	.....	
80	35	♂	159	..	..	+	..	..	..	..	F	.....	Incomplete stellate cataract in both eyes and some opacities situated nasally in left eye
			160	..	+	+	..	..	..	..	F	.....	
81	38	♂	161	..	+	..	..	..	+	..	F	.....	
			162	..	+	..	..	..	+	..	F	.....	
82	25	♂	163	..	+	..	..	..	+	..	F	.....	
			164	..	+	..	..	..	+	..	F	.....	
83	22	♂	165	..	+	..	+	..	..	..	F	.....	Cortical opacities situated mainly inferiorly and nasally
			166	..	+	..	..	..	..	..	F	.....	
84	36	♀	167	..	+	..	..	..	+	..	F	.....	Nuclear relief
			168	..	+	..	..	..	..	..	F	.....	Nuclear relief
85	36	♀	169	..	..	..	..	..	..	+	F	.....	Nuclear relief
			170	..	+	..	..	..	+	..	F	.....	Nuclear relief
86	26	♂	171	..	+	..	+	..	..	..	F	.....	Beginning coronary opacities
			172	..	+	..	+	..	..	..	F	.....	
87	24	♂	173	..	..	..	+	..	..	..	F	P. S.	
			174	..	..	..	+	..	..	..	..	.....	
88	25	♂	175	..	+	..	+	..	..	+	F	P. S., P. M.	
			176	..	+	..	+	..	..	+	F	P. M.	
89	21	♂	177	..	+	..	..	..	+	..	F	.....	Opacities situated mainly nasally
			178	..	+	..	..	..	+	+	F	.....	Opacities situated mainly nasally
90	25	♂	179	+	+	..	..	..	+	..	N	.....	Beginning peripheral concentric lamellar opacities and coronary cataracts
			180	..	+	..	..	..	+	..	N	.....	
91	37	♂	181	..	+	..	..	+	..	..	F	.....	Nuclear relief
			182	..	+	..	..	..	+	+	F	.....	Nuclear relief
92	29	♂	183	..	+	+	+	+	+	+	N	.....	Beginning bilateral opacities
			184	..	+	..	..	+	+	..	N	.....	Peripheral concentric lamellar opacities
93	18	♂	185	..	+	..	..	..	+	..	F	.....	Peripheral concentric lamellar opacities
			186	..	+	..	..	..	+	..	F	.....	Peripheral concentric lamellar opacities
94	30	♂	187	+	+	..	..	..	+	..	F	.....	
			188	+	..	..	..	..	+	..	F	.....	
95	23	♂	189	+	..	+	..	..	..	..	F	.....	Stellate opacities in both lenses
			190	+	..	+	..	..	..	..	F	.....	
96	27	♂	191	..	+	..	+	..	+	..	F	.....	Opacities situated entirely nasally
			192	..	+	..	..	..	..	..	F	.....	Opacities situated mainly nasally
97	26	♂	193	..	+	..	..	..	+	..	F	.....	Early peripheral concentric lamellar opacities
			194	..	+	..	..	..	+	+	F	.....	Early peripheral concentric lamellar opacities
98	19	♂	195	..	..	..	+	..	..	..	F	.....	
			196	..	+	+	..	+	+	+	F	P. S.	
99	26	♂	197	+	+	..	..	..	+	..	F	.....	
			198	..	+	..	..	..	+	..	F	.....	
100	26	♂	199	+	+	..	+	..	+	..	N	P. S., P. M.	Peripheral concentric lamellar opacities
			200	..	..	..	+	..	+	..	F	P. S.	
101	39	♂	201	..	+	..	..	+	+	..	N	.....	Opacities situated mainly nasally
			202	..	+	..	..	..	+	..	N	.....	
102	23	♂	203	+	+	..	..	..	+	..	N	P. S.	Many fine punctiform opacities under anterior capsule; deeper opacities situated mainly nasally
			204	+	+	..	..	+	+	+	N	.....	
103	31	♂	205	..	+	..	..	..	+	..	N	.....	Opacities situated mainly nasally
			206	..	+	..	..	..	+	+	N	.....	Peripheral concentric lamellar opacities
104	22	♂	207	..	+	..	+	..	..	..	F	P. M.	Opacities situated nasally only
			208	..	+	..	..	..	..	..	F	.....	Opacities situated nasally only
105	33	♂	209	..	+	..	..	..	+	..	F	.....	Opacities situated mainly nasally
			210	..	+	+	+	..	+	..	F	P. S.	Opacities situated mainly nasally
106	23	♂	211	+	+	..	..	..	+	+	N	.....	Cataracta cerulea
			212	+	+	..	..	..	+	+	N	.....	Cataracta cerulea
107	38	♂	213	..	+	..	+	..	+	..	N	.....	Opacities situated mainly nasally
			214	..	+	..	+	..	+	..	N	.....	Opacities situated mainly nasally
108	20	♂	215	+	+	..	..	..	..	..	F	.....	
			216	+	+	..	..	..	..	..	F	.....	
109	27	♂	217	..	+	+	..	+	..	..	F	.....	
			218	..	+	+	..	+	..	..	F	.....	
110	24	♀	219	..	..	..	+	..	..	+	F	.....	
			220	..	+	..	..	..	+	..	F	.....	Opacities situated mainly nasally
111	22	♂	221	..	+	..	..	..	+	..	N	.....	
			222	..	+	+	..	..	..	..	F	.....	
112	23	♂	223	..	+	..	..	..	+	+	F	P. M.	
			224	..	+	..	+	..	..	..	F	.....	A striate opacity also present nasally
113	38	♂	225	..	+	..	..	..	+	+	N	.....	Opacities situated mainly nasally; nuclear relief
			226	+	+	..	..	..	+	+	N	.....	1 linear opacity and many punctate opacities situated nasally; nuclear relief
114	35	♂	227	..	+	..	..	..	..	..	N	.....	Opacities situated mainly inferiorly and nasally
			228	..	+	..	..	..	..	+	F	.....	

* See text for interpretation of symbols.

Location of Opacities in the Crystalline Lens—Continued

Patient	Age, Yr.	Sex	Eye	A*	B	C	D	E	F	G	H	I	Comment
115	40	♂	229	..	−	+	..	..	..	..	F	.....	Triradiate opacities; other opacities situated mainly nasally; nuclear relief also present
			230	..	+	+	..	..	..	..	F	.....	Triradiate opacities
116	21	♂	231	..	..	..	+	+	..	..	F	P. M.	Opacities situated mainly nasally
			232	..	−	..	..	+	−	..	F	.....	Opacities situated mainly nasally
117	26	♂	233	..	+	..	+	..	+	..	N	.....	Opacities situated mainly nasally
			234	..	−	..	..	..	+	..	N	P. S.	Opacities situated mainly nasally; also cataract cerulea present
118	18	♂	235	..	..	..	..	+	−	..	F	.....	
			236	..	..	..	..	+	+	..	F	.....	
119	28	♂	237	..	−	−	+	..	−	..	F	.....	Krukenberg spindle on cornea; opacities in lens situated mainly nasally
			238	..	..	..	..	..	..	..	..	.....	Lens clear
120	36	♂	239	..	+	+	..	..	+	..	F	.....	Opacities situated mainly nasally; also triradiate opacities
			240	..	..	+	..	..	..	..	F	.....	Triradiate opacities
121	27	♂	241	..	+	..	..	..	+	..	F	P. S.	
			242	..	−	..	..	..	+	..	F	.....	
122	29	♂	243	..	+	..	..	..	..	..	F	.....	Opacities situated nasally
			244	..	..	+	..	..	..	..	F	.....	
123	30	♂	245	..	+	..	..	..	+	..	N	.....	Most opacities situated nasally in both eyes
			246	..	+	..	..	..	+	..	N	.....	
124	28	♂	247	+	−	..	..	..	−	+	N	.....	Cataracta coronaria and cerulea
			248	+	+	..	..	..	+	+	N	.....	Cataracta coronaria and cerulea
125	26	♂	249	+	+	..	..	..	+	+	F	.....	
			250	+	+	..	..	..	+	+	F	.....	
126	40	♂	251	+	−	..	..	..	−	+	N	.....	Cataracta coronaria
			252	+	+	..	..	..	+	+	N	.....	Cataracta coronaria
127	27	♀	253	..	−	..	..	..	..	..	F	.....	Both punctate and striate opacities situated nasally
			254	..	..	+	..	..	..	+	F	.....	
128	23	♀	255	..	−	..	..	..	+	..	F	.....	
			256	..	−	..	+	..	−	..	F	.....	
129	27	♂	257	+	..	..	..	..	−	..	F	.....	
			258	..	−	+	..	..	+	..	N	.....	Opacities situated nasally and inferiorly
130	28	♂	159	..	+	..	..	..	+	..	F	.....	
			260	..	+	..	+	..	−	..	F	P. M.	
131	24	♀	261	..	..	+	..	..	..	..	F	P. S.	Triradiate cataract
			262	..	..	+	..	..	..	..	F	P. S.	
132	23	♀	263	..	+	..	..	..	−	..	N	.....	Peripheral concentric lamellar opacities
			264	..	+	+	..	+	+	+	N	P. M.	
133	22	♀	265	..	..	..	..	..	..	+	F	P. S.	
			266	..	+	..	..	..	+	..	F	.....	
134	24	♂	267	+	+	..	..	..	..	..	F	.....	
			268	..	+	..	..	..	+	..	F	.....	
135	22	♀	269	..	−	..	..	..	..	+	F	.....	Opacities situated mainly nasally
			270	..	+	..	..	..	..	..	F	.....	Opacities situated mainly nasally
136	23	♂	271	..	+	..	..	..	+	..	F	.....	
			272	..	−	+	..	..	−	+	F	.....	Opacities situated entirely nasally
137	29	♂	273	..	+	..	..	+	+	..	F	.....	Opacities in nasal portions
			274	..	+	..	..	..	−	..	F	P. S.	Opacities in nasal portions
138	19	♂	275	+	+	..	..	..	+	..	N	.....	Opacities situated mainly nasally
			276	..	+	..	..	..	..	..	F	.....	Opacities situated mainly nasally
139	20	♂	277	..	..	..	+	..	+	..	F	.....	
			278	..	..	..	..	..	+	..	F	.....	
140	18	♂	279	..	..	..	..	+	+	..	F	.....	
			280	..	..	..	..	..	−	..	F	.....	Nasal opacity only
141	20	♂	281	..	..	..	..	..	−	..	F	.....	
			282	..	..	..	..	..	+	..	F	.....	
142	23	♂	283	..	..	+	..	..	−	+	N	.....	
			284	..	..	..	+	..	−	+	F	.....	
143	25	♂	285	..	+	..	..	..	+	..	F	.....	
			286	..	+	..	..	..	+	..	F	.....	
144	20	♂	287	+	+	..	..	..	..	..	F	P. M.	
			288	+	+	..	..	..	..	..	..	.....	
145	29	♂	289	..	..	..	+	+	+	..	F	.....	
			290	..	+	..	..	+	..	..	F	.....	Opacities situated entirely nasally
146	21	♂	291	+	..	..	..	..	..	..	F	P. M.	Capsular opacity connected to pupillary strands
			292	..	..	..	..	+	..	..	F	.....	
147	25	♂	293	..	+	..	..	..	+	..	F	.....	Punctate opacity situated nasally
			294	..	+	..	..	..	..	..	F	.....	Opacities situated mainly nasally; also bilaterally
148	31	♂	295	..	+	..	..	..	+	..	N	.....	Cataracta cerulea
			296	..	+	..	..	..	+	..	N	.....	
149	21	♂	297	..	+	..	..	..	+	+	F	.....	Opacities situated mainly nasally
			298	..	+	..	..	+	..	..	F	.....	
150	21	♂	299	..	..	..	..	..	+	+	F	P. S.	
			300	..	..	..	+	..	+	+	F	.....	

* See text for interpretation of symbols.

or 15 per cent, had opacities in the anterior Y region; 6 eyes, or 21 per cent, in the central dark interval, and 56 eyes, or 19 per cent, in the posterior Y region). Like its anterior counterpart, the deep posterior cortex had numerous opacities (179 eyes, or 60 per cent, had opacities between the posterior Y region and the posterior band of disjunction). Finally, in the posterior sections of the lens substance in all other eyes.

Coronary cataracts were found bilaterally in 6 subjects (fig. 2); in 2 of them the opacities were well developed and were associated with cataracta cerulea, while in 4 the coronary opacities were poorly developed. Peripheral concentric lamellar opacities were present in 15 eyes (5 opacities being bilateral and 5 unilateral).

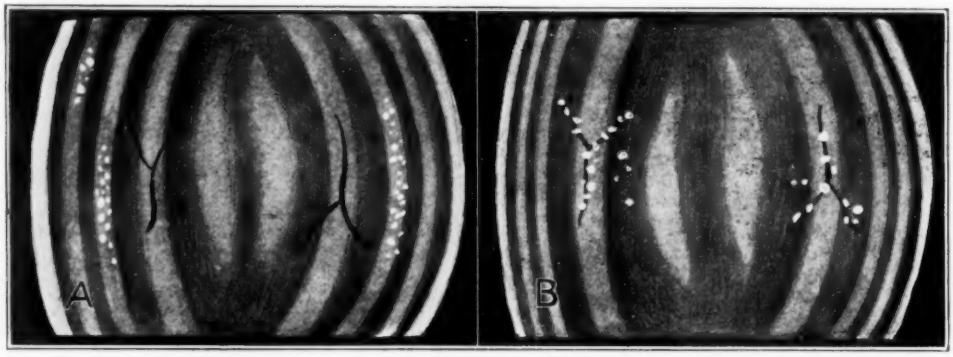

Fig. 1.—*A*, punctate opacities in the upper portion of the anterior band of disjunction and axial opacities in the anterior and posterior adult nuclear bands. *B*, punctate opacities in the regions of the anterior and posterior Y sutures.

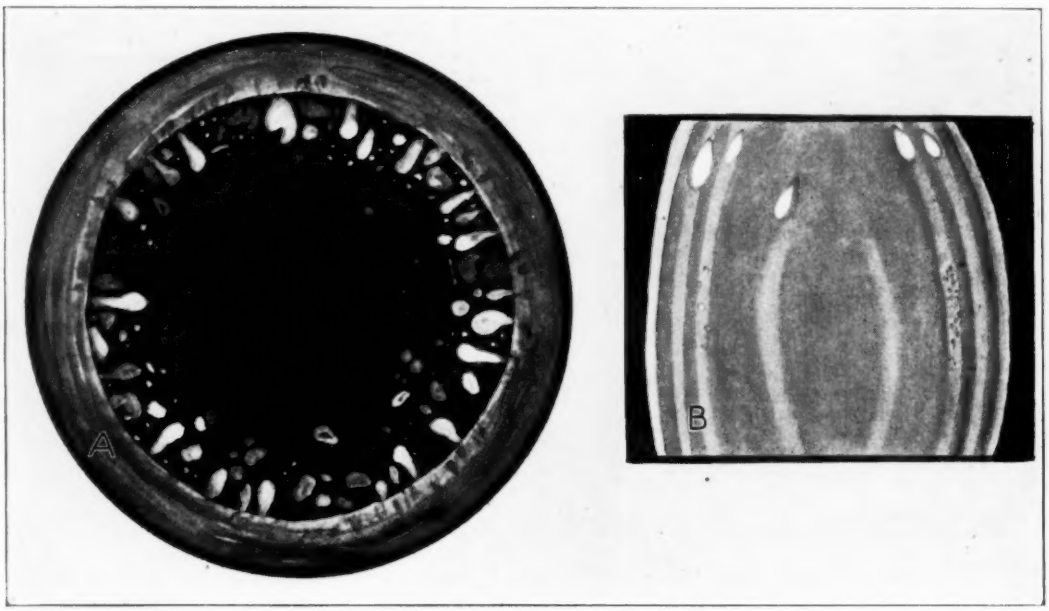

Fig. 2.—Cataracta coronaria: *A*, ophthalmoscopic section; *B*, optical section.

superficial section the number of opacities decreased, approximating the number found in the corresponding anterior layer (70 eyes, or 23 per cent had such opacities).

In 65 eyes (22 per cent) the opacities were either exclusively or preponderantly in the nasal portions of the lens. In 12 other eyes the opacities were mainly in the inferior and nasal portions. The opacities were uniformly distributed peripherally or scattered throughout the various

Of 115 subjects (230 eyes) only 8 subjects (16 eyes) showed nuclear sclerosis, and all the subjects in this group were over 35 years of age. In 219 eyes opacities were few; the average age of the subjects having few opacities was 25 years. Eighty-one eyes had numerous punctate opacities; the average age of the subjects was 30 years. Nuclear relief was observed in 8 (16 eyes) of 115 subjects. All persons showing nuclear relief were over 35 years of age.

COMMENT

Nummular, annular and punctiform opacities measuring from 20 to 100 microns were found in all but 8 of 300 eyes examined with the slit lamp. Since these opacities increase in number with age, they must be considered forms of presenile cataract. However, opacities occur so commonly in otherwise healthy persons that their presence is considered normal. Cataracta coronaria, cataracta cerulea and cataracta viridis are included here because they are so frequently associated with presenile opacities.

Hess [4] expressed the opinion that the site of predilection for incipient senile cataract is the immediate subcapsular layer. The present observations indicate that the most common site of punctate opacities is between the band of disjunction and the region of the Y suture, particularly anteriorly. Later, as the lens ages, the opacities increase in number and involve the outer cortex. If the opacities are in the axial region and become dense, the visual acuity diminishes.

At times the punctate opacities in the periphery form concentric lamellar layers (fig. 3 *A*). Vogt stated that an arrangement of large yellowish gray layers about the nuclear equator is found only in elderly subjects. The average age of the persons showing the incipient stage of this condition in this series was 26 years. A frequent associated finding was a widening and intensification of the anterior and posterior bands of the adult nucleus at the equator.

Punctate opacities following the pattern of the anterior axial system of cortical sutures may evolve into an opacity shaped like the antlers of a deer (fig. 3 *B*). Punctate opacities on the anterior cortical suture system, as this form of presenile cataract is called, readily escape detection during a routine examination, even with a slit lamp, because the opacities are very minute. Vogt stated that the youngest patient observed by him with this type of cataract was 36 years of age. The condition illustrated in figure 3 *B* was observed in a 25 year old soldier. That punctate opacities on the anterior cortical suture system are true forms of senile cataract is proved by the fact that cuneiform opacities, which are definitely a form of senile cataract, were also present.

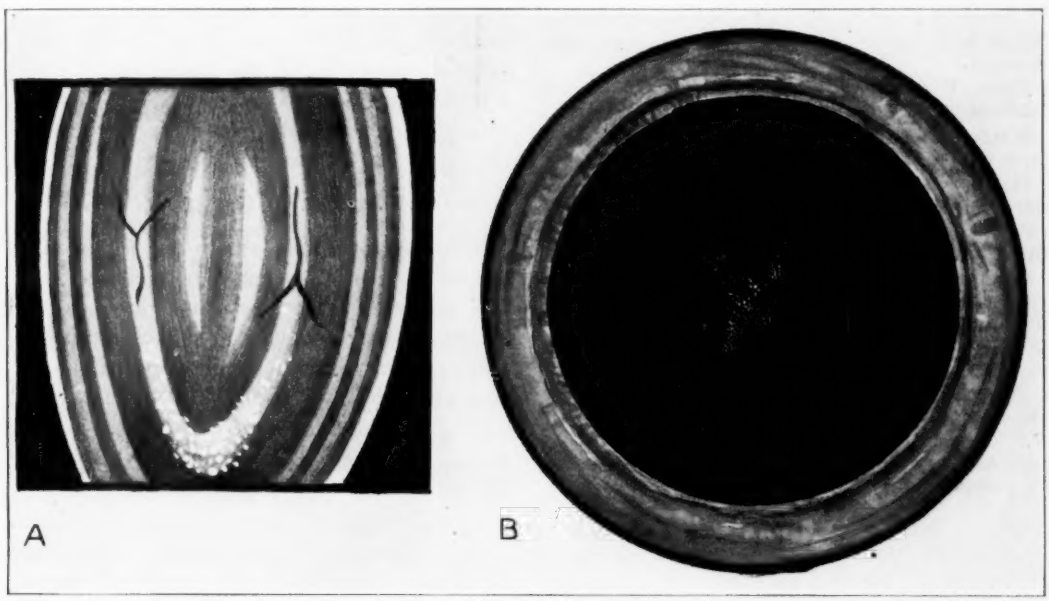

Fig. 3.—*A*, punctate opacities in the form of peripheral concentric lamellar layers. *B*, punctate opacities on the anterior cortical suture system.

Coronary opacities were present in 4 per cent of the eyes, a figure in close agreement with the results of the investigation by Kirby,[5] who found that these opacities formed 4.5 per cent of all cataracts. Vogt, on the other hand, stated that coronary cataracts are found in 25 per cent of all persons past the age of puberty.

Case 38 (see table) raises the question of the causation of anterior rosette cortical cataract.

4. Hess, C.: Pathologie und Therapie des Linsensystems, in Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, ed. 3, Leipzig, Wilhelm Engelmann, 1911, pt. 2, chap. 9.

5. Kirby, D. B.: A Study of Standards for Judging of the Progress or Arrest of Cataract, Tr. Am. Acad. Ophth. **32**:203-230, 1927.

This cataract is usually attributed to trauma. The subject of this report, a 27 year old soldier, said he had never received an injury to the involved eye. Slit lamp examination supported his contention, for objective signs of trauma were absent. Similar cases have been reported by Rauh,[6] Nordmann[7] and Handmann.[8]

Although this report concerns itself with opacities in the crystalline lens, the number of eyes showing pigmented capsular stars or pigmented strands was also noted (table, column I). Thirty-three eyes showed pigmented stars on the surface of the lens, and 23 showed pupillary strands. Gallemaerts and Kleefeld[9] reported that embryonal pupillary remnants were observed by them in 20 per cent of all their cases. A tendency to absorption is indicated by the decreased incidence with age.[10] One instance of pigmented striae on the anterior surface of the lens in the retroiridal region was observed. The case referred to is included in another report.[11]

6. Rauh, W.: Blatt- oder rosettenförmige Stare, Klin. Monatsbl. f. Augenh. **84**:766-773, 1930.

7. Nordmann, J.: A propos de certaines formes de cataracte en rosace, Arch. d'opht. **48**:392-402, 1931.

8. Handmann, M.: Ueber den blatt- oder rosettenförmigen vorderen Rindenstar, eine nichttraumatische stationäre Starform unbekannten Ursprunges, Klin. Monatsbl. f. Augenh. **78**:31-43, 1927.

9. Gallemaerts, E., and Kleefeld, G.: L'étude microscopique du fond de l'oeil vivant, Ann. d'oculi. **159**:264-274, 1922.

10. Vogt.[2] Hirschberg, J.: Ueber langsame Rückbildung der persistirenden Pupillenhaut, Centralbl. f. prakt. Augenh. **28**:103-105, 1904. Bruckner, A.: Ueber Persistenz von Resten der Tunica vasculosa lentis, Arch. f. Augenh. (supp.) **56**:5-149, 1907. Bellows, J.: Cataract and Anomalies of the Lens, St. Louis, C. V. Mosby Company, 1944.

SUMMARY

Three hundred eyes of persons between 18 and 40 years of age were examined by means of slit lamp microscopy. All but 8 eyes showed some form of punctate opacities. In 4 per cent of the eyes the opacities were associated with coronary cataracts. Punctate opacities were found in all the layers of the lens, but were far more common between the bands of disjunction and the region of the Y sutures, being more numerous anteriorly than posteriorly. Not uncommonly the opacities arranged themselves in concentric layers surrounding the nucleus. These opacities are precursors of peripheral concentric lamellar opacities of the senile lens, which are a true form of senile cataract. At times punctate opacities of unusually small size are present in the anterior cortical suture system.

CONCLUSIONS

Punctate opacities, which are found in nearly all adult lenses, increase in number with the age of the subject. They precede nuclear relief, increase in the elementary stripes composing the adult nuclear band and yellowing of the nucleus as a sign of aging of the lens.

11. Bellows, J.: Pigmented Lines in Retroiridal Region of Anterior Capsule of Lens, Arch. Ophth. **32**: 483-484 (Dec.) 1944.

TOTAL HERPES ZOSTER OF THE OPHTHALMIC, MAXILLARY AND MANDIBULAR DIVISIONS OF THE TRIGEMINAL NERVE

REPORT OF A CASE IN WHICH THERE WAS ALSO INVOLVEMENT OF THE GENICULATE GANGLION AND THE VESTIBULAR PORTION OF THE EIGHTH CRANIAL NERVE

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Herpes zoster is a not rare acute infection of the posterior root ganglions with signs in the segmental distribution of the nerve roots involved,[1] while, contrariwise, herpes zoster ophthalmicus, or herpes zoster of a gasserian ganglion, a homologue of a posterior root ganglion, is apparently a rather rare disease; indeed, it is so rare that Rice[2] stated that no cases of ophthalmic herpes zoster were mentioned, for example, in the report of one of the largest ophthalmologic and otologic hospitals in the United States, in which over 100,000 patients with ocular disease were treated in 1922. On the other hand, Gundersen,[3] in searching for cases of herpes zoster ophthalmicus, found 10 per annum at the Massachusetts Eye and Ear Infirmary, in Boston, over a five year period.

From the standpoint of the dermatologist, who will inevitably see ophthalmic herpes zoster initially, the common sites of localization of herpes zoster are an intercostal nerve, the trigeminal nerve (particularly the first branch, herpes zoster ophthalmicus) and the sensory nerves of the extremities. Herpes zoster of the arm or of the leg is unusual and hence often not diagnosed.[4]

Pillsbury, Sulzberger and Livingood[4] stated that herpes zoster may occur as a concomitant manifestation with the leukemias, various blood dyscrasias, Hodgkin's granuloma and malignant visceral tumors and is not uncommon in tabetic syphilis. They grouped under the following five subdivisions the less common forms of herpes zoster: (1) gangrenous herpes zoster, with necrotic and destructive lesions, a severe form of which can occur in any region but which is most common in the region of the ophthalmic nerve; (2) hemorrhagic herpes zoster, with blood-containing vesicles; (3) bullous herpes zoster; (4) bilateral herpes zoster, either symmetric or asymmetric, which is extremely rare but which, contrary to certain superstitions, is not fatal[4]; (5) generalized herpes zoster, in which the eruption consists of scattered discrete papules and vesicles and is accompanied by headache, fever and malaise. There may be lesions of the mucous membrane, with the entire picture resembling chickenpox. Only epidemiologic considerations and the presence of concomitant typical herpes zoster following the course of a nerve will permit differentiation between ordinary chickenpox and this type of herpes zoster.[4]

Herpes zoster is usually limited to one of the divisions of the fifth cranial nerve,[5] although it rarely involves the nucleus of the sensory root of the seventh cranial nerve. This enabled Hunt[6] to delineate the distribution of the cutaneous portion of the geniculate ganglion, since the herpetic cutaneous eruption is found in the area of distribution of that ganglion, that is, in the cleft between the ear and the face and on the membrana tympani, the auditory canal walls, the concha, the helix and anthelix and the tragus and antitragus. The cutaneous herpetiform response of the geniculate ganglion to herpes zoster apparently may be total or minimal. It can be stated dogmatically that herpes zoster involving not only the ophthalmic but the maxillary and mandibular divisions of the fifth cranial nerve is rare, judged by the total absence of reported cases in the literature. Axiomatically, total herpes zoster of the trigeminal nerve with concomitant cutaneous involvement of the geniculate ganglion, the combination of which likewise has not been

1. Meakins, J. C.: The Practice of Medicine, ed. 4, St. Louis, C. V. Mosby Company, 1944.

2. Rice, G. W.: Herpes Zoster Ophthalmicus, Eye, Ear, Nose & Throat Monthly **2**:265, 1923-1924.

3. Gundersen, T.: Convalescent Blood for Treatment of Herpes Zoster Ophthalmicus, Arch. Ophth. **24**:132 (July) 1940.

4. Pillsbury, D.; Sulzberger, M., and Livingood, C.: Manual of Dermatology, Philadelphia, W. B. Saunders Company, 1943.

5. Grinker, R. R.: Neurology, ed. 3, Springfield, Ill., Charles C Thomas, Publisher, 1943.

6. Hunt, J. R.: Herpetic Inflammation of the Geniculate Ganglion, J. Nerv. & Ment. Dis. **34**:73 (Feb.) 1907.

reported in the literature, is rare indeed, although Fuchs, cited by Graves,[7] reported 2 cases in which with herpes zoster ophthalmicus, that is, with manifestations of the frontal branch only, there was concurrent involvement of the seventh cranial nerve with resulting lagophthalmos and keratitis. This combination is not rare, nor is that of herpes zoster ophthalmicus with involvement of the third, fourth, sixth and seventh cranial nerves with ocular palsy. Cases of this condition have been reported fairly frequently. Moore [8] found that in his cases in which herpes zoster was associated with ocular palsy involvement of the third cranial nerve was by far the most common phenomenon, viz., in 74 per cent.

At this point it is worth while to draw attention to an equivocal report of Agnello,[9] who, in discussing 3 cases of herpes zoster, described in 1 a papular eruption of the forehead, in a second vesicles on the skin in the middle of the forehead and in a third vesicles on the left side of the face and forehead. He said that all three branches of the left trigeminus nerve were affected, a statement which is extremely hard to reconcile with the fact that no cutaneous herpetiform eruption along the maxillary and mandibular nerve trunks was described in his paper.

What, then, is herpes zoster? It occurs as two types, epidemic, idiopathic herpes zoster, arising, de novo, and symptomatic herpes zoster. The latter may be found in a patient, for example, with some antecedent factor, such as fracture of the basal portion of the skull, meningitis of syphilitic or tuberculous origin or tumor of the pons, in whom symptomatic herpes zoster then develops by reason of the virus, which the patient is carrying, attacking the injured fifth cranial nerve, the gasserian ganglion or the central connections of the fifth cranial nerve. There is, to be sure, no difference between the causal virus of the idiopathic and of the symptomatic type except that in the epidemic type the attack arises spontaneously in unprepared soil while in the symptomatic type preexisting trauma to the nerve is postulated.[7] In the latter type, then, the virus has a fertile soil in which to thrive.

Brain reported symptomatic herpes zoster as a sequela of subarachnoid hemorrhage, while other writers incriminated such variants as pneumonia, carbon monoxide and arsenic as etiologic factors. In all cases of trigeminal herpes zoster, whether of the idiopathic or the symptomatic type, however, one thing is certain, that the ophthalmic branch is always involved and the other branches with extreme rarity. If cutaneous herpetic involvement were the whole story, the disease could well fall within the province of the dermatologist, but, unfortunately, intraocular complications occur in 60 per cent of the cases, with the cornea allegedly affected in 35 per cent of these. Graves,[7] indeed, expressed the opinion that slit lamp examination would reveal deep epithelial changes in practically all cases; hence the importance of the disease to ophthalmologists is apparent.

HISTORICAL REVIEW

A short review of the historic aspects of the disease may not be amiss. In 1866 Hutchinson [10] published his classic description of the disease, while a year later Bowman [11] described several cases of herpes frontalis seu ophthalmicus, with illustrations in 1 case, showing residual facial pitting and scarring. In a second case described by Bowman diplopia occurred, while in a third case one sequel was atrophy of the optic nerve. Bowman in his writings stressed the fact that the supraorbital and supratrochlear divisions of the frontal branch of the ophthalmic division of the trigeminal nerve are most commonly involved, with the nasociliary branch of the ophthalmic nerve usually escaping.

In Hutchinson's day the disease was confused with erysipelas as it is today, for that matter. Hutchinson's dictums on this point were in the eighties popular examination questions in the hospitals in London. These dictums bear repetition after some seventy-eight years.

> Herpes frontalis is always limited to one side. It never transgresses the median line of the forehead and nose. It never affects the cheek although there may be some sympathetic oedema of contiguity. There is less general swelling of the skin than in erysipelas, much more pain and less constitutional disturbance in herpes than in erysipelas.

A corollary of this dictum followed, which stated that "if there is involvement of the nasociliary nerve and vesicles form on the side of the nose the eye is most likely to be involved," a statement which has been valid in 6 cases seen

7. Graves, B., in Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936.

8. Moore, R. F.: Ocular Manifestations of Lesions of the Fifth Cranial Nerve, Brit. M. J. **2**:783 (Oct. 29) 1932.

9. Agnello, F.: Clinical Varieties and Ocular Lesions of Herpes Zoster, Riv. oto-neuro-oftal. **11**:172 (March-April) 1934.

10. Hutchinson, J.: Clinical Report on Herpes Zoster Frontalis, Roy. London Ophth. Hosp. Rep. **5**:191, 1865-1866; Exact Portion Affected by Herpes, ibid. **6**:48, 1867.

11. Bowman, W.: Cases of Zoster, Roy. London Ophth. Hosp. Rep. **6**:1, 1867-1869.

by me since 1939 but the universality of which has been denied. Not so noteworthy is Hutchinson's other statement that when the tip of the nose is involved the eye will be lost—a conclusion which was not validated by Friedenwald [12] or in my present case, in which the nose, tip and all, both "within and without," was involved.

Another dictum, that zoster never affects the cheek, apparently stood unchallenged until 1900, when Head and Campbell [13] reported a case of idiopathic herpes zoster involving the mandibular branch in which the cutaneous manifestation did, obviously, affect the cheek. And sixty years after the enunciation of Hutchinson's dictum, Paton [14] reported a case in which the herpetiform eruption affected both the forehead and the cheek, the first and second divisions of the trigeminal nerve being cutaneously involved. Obviously, then, with the two exceptions noted, one in 1900 and the other in 1926, if Agnello's equivocal, and not easily interpreted, report is dismissed, trigeminal herpes zoster meant, in effect, zoster with a herpetiform eruption along the course of one or more of the three branches of the ophthalmic division of the trigeminal nerve only, that is, the lacrimal, the frontal (supraorbital and supratrochlear) and the nasociliary nerves. In the case presented in this paper, in which all three of the divisions of the trigeminal nerve, the ophthalmic (lacrimal, frontal [supratrochlear and supraorbital] and nasociliary), the maxillary and the mandibular, exhibited cutaneous manifestations, there was not only concomitant erythema and herpes (Hunt's herpes) due to involvement of the geniculate ganglion but some preceding evidence of involvement of the vestibular branch of the eighth cranial nerve, with the patient displaying symptomatic manifestations of tinnitus, nystagmus and partial loss of balance. After a review of the literature, therefore, I feel that in the case to be presented the neuro-ophthalmologic features are unique enough to interest ophthalmologists.

The age incidence of herpes zoster ophthalmicus has been stated to be 55 years (Lodge and Lodge [15]). In 6 cases observed by me in private practice in the past five years, 5 patients were under 45 years and 1 was a woman of 70 years. Fisher (cited by Paton) observed the condition in an infant 4½ months old, and Koch,[16] in reporting in 1939 on a patient aged 5½ years, mentioned that this was the earliest age at which the condition had been observed at the Mayo Clinic. The impression is general that ophthalmic herpes zoster occurs most commonly in aged and debilitated persons. In my limited experience this has not been the case.

The patient in the case to be presented was 44 and a working man in extremely robust health, with no known exposure to varicella; in but 1 case in my recent experience could the victim be classed as either aged or debilitated, and in no single case was a previous history of contact with varicella found, despite questioning.

ANATOMIC CONSIDERATIONS

The trigeminal nerve is made up of both motor (to muscles of mastication) and sensory roots and is therefore a mixed nerve. Root fibers from the second division mainly descend to the second cervical segment via the pons and the medulla, with the fibers from the ophthalmic division descending most caudad. The gasserian, or trigeminal, ganglion, which is a primary sensory and trophic station, lies on the pars petrosa of the temporal bone, in the middle fossa in the floor of the lateral part of the cavernous sinus, and divides into the ophthalmic branch, with the associated ciliary ganglion, the maxillary branch, with the associated sphenopalatine ganglion and the mandibular branch, with the associated otic and submaxillary ganglions. The sphenopalatine ganglion, which supplies the mucous membranes of the nose and palate, is connected with the seventh cranial nerve, while the geniculate ganglion, from which the sensory root of the facial nerve arises, is in much more direct connection with the seventh cranial nerve than with the eighth cranial nerve, with which it communicates by the small branch known as the pars intermedia. The trigeminal nerve itself is related to the seventh cranial nerve by means of the superficial petrosal nerves, the large and the small. The ophthalmic division of the trigeminal nerve innervates the lids, conjunctiva, iris, cornea and root of the nose, while the external ear is innervated not only by the fifth cranial nerve but by the seventh cranial nerve, the internal meatus being supplied by the seventh and the posterior wall of the external acoustic meatus by the tenth cranial (vagus) nerve. The maxillary nerve transmits sensibilities from the cheeks, nasal fossa, palate and upper teeth. The mandibular nerve brings in sensibili-

12. Friedenwald, J. S.: Report of Case of Herpes Zoster Ophthalmicus Treated with Convalescent Serum, Bull. Johns Hopkins Hosp. **45**:103 (Aug.) 1929.

13. Head, H., and Campbell, A. W.: The Pathology of Herpes Zoster, Brain **23**:353, 1900.

14. Paton, L.: The Trigeminal and Its Ocular Lesions, Brit. J. Ophth. **10**:305 (June) 1926.

15. Lodge, S., and Lodge, W.: Herpes Zoster Ophthalmicus, Tr. Ophth. Soc. U. Kingdom **43**:659, 1923.

16. Koch, F. L. P.: Herpes Zoster Ophthalmicus, Arch. Ophth. **21**:118 (Jan.) 1939.

ties from the chin, lower teeth, tongue and temporal region. Within the semilunar ganglion a rearrangement of fibers from a somatotropic to a physiologic plan occurs, and when the trigeminal tracts course through the medulla they carry specific types of sensibility from all the peripheral area.[17] The peripheral fibers of the seventh cranial nerve (facial) after arising in the geniculate ganglion are incorporated in the chorda tympani and come from the taste buds of the anterior two thirds of the tongue. Efferent fibers arising in the medulla are incorporated with the sensory root to form the composite glossopalatine nerve. Through the chorda tympani these efferent fibers supply the submaxillary ganglion which supplies the submaxillary gland.[17]

The seventh nerve, then, is much more intimately connected with the geniculate ganglion than with the eighth nerve, for which reason facial paresis is much more common in herpes zoster than is symptomatic involvement of the vestibular branch of the eighth nerve.

PATHOLOGIC CONSIDERATIONS OF HERPES ZOSTER

Primary neuritis of the trigeminal nerve, if one excludes tic douloureux and neuralgia, is rare.[18] The ophthalmic division of the trigeminal nerve, however, is especially apt to be affected by aneurysms of the carotid artery and by thrombosis of the cavernous sinus, while the trigeminal nerve as a whole may be involved by gummatous syphilis, basilar meningitis, fracture of the skull, tuberculosis and vascular pontile disease. As previously stated, there are two recognized types of the disease, a primary idiopathic involvement of the ganglions, occurring in either epidemic or sporadic form, and a symptomatic type, which appears during the course of an infectious disease, such as encephalitis (rare), or by extension by contiguity into the ganglion of a neighboring pathologic process. The virus of herpes zoster has apparently never been transmitted to animals.[7] The herpetiform cutaneous lesions are probably due to antidromic impulses which cause the liberation of histamine-like bodies, and axon reflexes allegedly cause the spread of the vasodilatation.[19] In this field of the viruses much remains to be learned. Is there a neurotropic as well as a dermotropic virus? Other unknown factors are the effect of resistance of tissue and the toxic effect of viruses, ignorance of which beclouds the picture. Is it possible that in dendritic keratitis, keratitis disciformis, herpes corneae and herpes zoster ophthalmicus herpetic viruses play a part?[7] Gruter, cited by Graves,[7] demonstrated a specific herpes virus, which when transferred from a herpetic lesion in man to a rabbit's cornea produced a vesicular lesion; the virus, it is believed, travels by way of the fifth nerve to cause encephalitis. It has long been surmised that varicella and herpes zoster are related, and with increasing knowledge of the viruses it has been assumed that for idiopathic herpes there is probably a transmissible virus possibly related to varicella.[20] Bokay, in 1888, noted a case of varicella occurring ten days after the patient's contact with herpes zoster. Pickard[21] expressed the opinion that the virus causing varicella and herpes zoster shows two phases, one representing herpes zoster and the other varicella. The zoster phase has its origin in a posterior root ganglion (it may spread to an anterior root, giving rise to the unusual muscular paralysis of herpes zoster), with extension and signs along the sensory nerves to fibrous tissue covered with epithelium, where the secondary or varicella phase appears. Blatt, Zeldes and Stein,[22] at the Cook County Hospital, Chicago, noted varicelliform eruptions with pyrexia in 4 of 140 children in two wards thirteen to twenty-one days after exposure to patients with herpes zoster. The authors were in doubt of the identity of the viruses, but they agreed with many former workers that there is a close relationship between herpes zoster and varicella. In none of my 6 recent cases has any antecedent contact with varicella been found, nor has varicella developed in any of the children who come in contact with patients with herpes zoster. The secondary cutaneous lesions of herpes zoster always show lymphocytic invasion, hemorrhage, epithelial necrosis and large vesicular cells of Unna, while primary herpes is an inflammatory disease of the ganglion with lymphocytic infiltration, swelling of the axis-cylinders and destruction of the nerve cells. If the pathologic process is sufficiently grave, a secondary wallerian degeneration occurs both in the dorsal roots and in the peripheral nerves. The ganglionic inflammation is therefore acute posterior poliomyelitis.[13]

17. Mettler, F. A.: Neuro-Anatomy, St. Louis, C. V. Mosby Company, 1942.

18. Wechsler, I. S.: Textbook of Clinical Neurology, ed. 5, Philadelphia, W. B. Saunders Company, 1943.

19. Parsons, J.: Diseases of the Eye, ed. 7, New York, The Macmillan Company, 1935.

20. Brain, R. W.: Zoster, Varicella and Encephalitis, Brit. M. J. **1**:81 (Jan. 17) 1931. Head and Campbell.[13]

21. Pickard, R.: The Causation of Herpes Ophthalmicus, Proc. Roy. Soc. Med. **28**:29 (Nov.) 1934.

22. Blatt, M. L.; Zeldes, M., and Stein, A. F.: Chicken Pox Following Contact with Herpes Zoster, J. Lab. & Clin. Med. **25**:951 (June) 1940.

Involvement of the eye of the affected side is usually explained by assuming that the disease extends by way of the long ciliary nerves which are given off from the nasal branch of the ophthalmic nerve, and thence, joining the short ciliary nerves from the ciliary ganglion, they pierce the sclerotic coat of the eyeball and pass forward between it and the choroid to the ciliary muscles, iris and cornea,[2] with keratitis, iritis, iridocyclitis and panophthalmitis as possible sequelae. Optic neuritis as a sequela of herpes zoster ophthalmicus is rare, for since Hutchinson's original report, in 1866, Duke-Elder [23] has collected only 10 reports of optic neuritis following herpes zoster; it occurred in 4 of 6 cases which I observed and studied. One wonders, therefore, if the difficulty of examining an acutely inflamed painful eye affected with herpes zoster does not explain this insignificant number of reported cases of involvement of the optic nerve. Gardilčić [24] described a case of herpes zoster in which, after the cornea of the eye was gravely involved, the eye became secondarily infected and a large hypopyon developed. Panophthalmitis resulted, and the eye was enucleated. Histologic study of this eye revealed that the small stumps of the ciliary nerves had an infiltration of plasma and small round cells; these infiltrated the sclera and the suprachoroidea and were scattered through the choroid. Furthermore, the ciliary blood vessels near the nerves were also surrounded by lymphocytes and plasma cells; there were two areas of necrosis in the sclera, which were stated by the author to be due to trophic disturbances in the diseased nerves.

Valière-Vialeix found that in 13 of 17 cases superficial keratitis with vesicular formation was rare while, on the other hand, the posterior and middle layers of the corneal stroma were affected.[25] Keratitis profunda, in short, was the common, rather than the rare, lesion, while in 1 case in their report there was also an Argyll Robertson pupil with no response to light but with retention of reaction to convergence. The Argyll Robertson pupil following herpes zoster is usually dilated, according to Wolff.[26]

Carmody,[27] in discussing the complications of herpes zoster ophthalmicus, classified them in four groups: keratitis, iridocylitis, muscular palsies and optic neuritis. In 50 per cent of the cases, according to Carmody, the globe was affected, and in the majority of these the cornea was damaged. He reported an interesting case in which herpes zoster ophthalmicus on the right side in a 40 year old syphilitic Negro was followed in three weeks by exophthalmos on the same side, which produced immobility of the globe. The cornea was severely involved; in this case one cannot be certain, of course, whether the condition was of the epidemic (idiopathic) type occurring in a syphilitic patient or whether it was of the symptomatic type due to syphilitic basilar meningitis, or possibly a gummatous process of syphilis.

Paralysis and atrophy of muscles, not necessarily related to the course of the cutaneous herpetic eruption, in cases of herpes zoster were reported by Taterka and O'Sullivan.[28]

The paralysis allegedly may occur as late as two months after the appearance of the herpetic eruption.

Denny-Brown and his co-workers [29] discussed the pathologic features of herpes zoster in 3 cases. In 2 cases of thoracic herpes zoster they reported in addition to severe neuritis degeneration of the involved motor and sensory roots, localized leptomeningitis and homolateral segmental poliomyelitis. In a third case of geniculate herpes in which the cutaneous manifestations involved the auriculo-occipital region they found necrotizing ganglionitis of the second cervical ganglion, homolateral segmental posterior poliomyelitis in the cervical portion of the cord and an inflammatory reaction in the medulla with motor neuritis of the facial nerve. In the geniculate ganglion itself no cellular destruction was seen, but in fibers of the paraganglionic facial nerve some lymphocytic infiltration was observed.

TREATMENT OF HERPES ZOSTER OPHTHALMICUS

For acute cutaneous lesions apparently any dry antiseptic powder, preferably sulfathiazole, will do. Medicaments are legion. Meakins,[1]

23. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1941.

24. Gardilčić, A.: Perineuritis and Periarteritis Ciliaris in a Recent Case of Herpes Zoster Ophthalmicus, Ztschr. f. Augenh. **92**:35 (May) 1937.

25. Valière-Vialeix, V.: Frequency of Parenchymatous Keratitis in Herpes Zoster: An Argyll-Robertson Pupil as a Sequel of Herpes, Ann. d'ocul. **168**:341 (May) 1931.

26. Wolff, E.: The Pathology of the Eye, Philadelphia, The Blakiston Company, 1943.

27. Carmody, R. F.: Herpes Zoster Ophthalmicus Complicated by Ophthalmoplegia and Exophthalmos, Arch. Ophth. **18**:707 (Nov.) 1937.

28. Taterka, J. H., and O'Sullivan, M. E.: Motor Complications of Herpes Zoster, J. A. M. A. **122**:737 (July 10) 1943.

29. Denny-Brown, D.; Adams, R., and Fitzgerald, P.: Pathologic Features of Herpes Zoster: Note on "Geniculate Herpes," Arch. Neurol. & Psychiat. **51**:216 (March) 1944.

following Sidlick,[30] suggested intramuscular injections of solution of posterior pituitary (0.5 to 1 cc.). He also suggested intravenous injections of sodium iodide, 10 cc. of the 20 per cent solution, repeated on the second, fourth and seventh days. This method was used by Ruggles. Solution of posterior pituitary obviously should be used with caution, as most patients with herpes zoster are reputedly elderly, with presumably an already impaired cardiac apparatus. Pillsbury suggested heavy doses of vitamin B complex and vitamin E.[4] Diphtheria antitoxin in doses of 5,000 units, injected every two days if necessary, was suggested by the Walkers.[31] Convalescent serum has been employed by both Friedenwald [12] and Gundersen.[3] The latter suggested the injection of 200 to 400 cc. of herpes zoster convalescent blood; the treatment should be initiated preferably before ocular infection occurs. Green [32] suggested autohemotherapy: Five to 10 cc. of whole blood, removed from the antecubital vein, is injected into the gluteal region every other day, accompanied by administration of 25 mg. of thiamine hydrochloride twice a week for six injections. Lillie,[33] in presenting 3 cases of herpes zoster, enthusiastically supported the therapeutic use of smallpox vaccine, a remedy which has been employed in past years by Green [34] and others in the treatment of herpes simplex and dendritic ulcer. As can be seen, many of these therapeutic suggestions for treating a disease of unknown but of suspected virus origin border on the irrational, although, as Friedenwald [12] sagely observed, cases of herpes zoster ophthalmicus are all too rare in the practice of any ophthalmologist to afford an adequate basis for the testing of diverse forms of therapy. For postherpetic pain, roentgen irradiation of the gasserian ganglion and pons has been recommended [5]; application of high voltage roentgen rays to the back in the region of the posterior nerve root, injection of alcohol or section of the sensory posterior root and section of the spinothalamic tract, which conveys impulses of pain from the involved area, are other suggestions.[1] All these methods have their proponents, but the problem of postherpetic pain has certainly not been solved. Peet [35] stated that postherpetic pain often persists for years, especially in aged persons, with symptoms identical with those described in many cases of tumor of the gasserian ganglion. He reported 2 cases of postherpetic trigeminal neuralgia in which there was persistence of pain after section of the sensory root of the gasserian ganglion; complete permanent relief, therefore, so certain with surgical treatment of major trigeminal neuralgia, cannot be assured the victim of herpes zoster with postherpetic pain. The anatomic basis of this clinical finding rests on the fact that a degree of cephalic sensitivity, particularly pain, may be preserved even though the semilunar ganglion of Gasser is entirely removed, for the sensory fibers accompany the cervical sympathetic plexus on the carotid artery and ultimately enter the cord in the region of the first thoracic segment.[17]

REPORT OF CASE

R. W., a man aged 44, presented himself June 29, 1944 with manifold complaints of burning pain in the right ear, a feeling of inability to balance himself, nausea and diplopia. His past medical history was noncontributory; there was no history of influenza or labyrinthitis. Neurologic examination showed diminished hearing in the right ear and horizontal nystagmus of both eyes with the fast component to the right. With these was a Romberg sign, with falling to the right. He said that this sense of imbalance had not been present prior to three days preceding his visit. No cerebellar symptoms were elicited; the pulse and respiration were both normal, and his temperature was slightly elevated. The referring physician was informed that the patient was probably suffering from an inflammatory process of the eighth cranial nerve and its vestibular ganglions, although a hemorrhage in the cerebellopontile angle could not be categorically dismissed. He was seen on the following day, June 30, at which time the nystagmus had diminished but the Romberg sign was still present. His complaint now was that he had severe pain in the right lower jaw and the right ear. At this time swelling of the postauricular and preauricular lymph nodes was obvious. The following day, July 1, the pain had advanced to the right side of the face and to the right side of the upper lip, and in the late afternoon a perceptible lag of the face was noticeable, combined with severe submaxillary adenopathy and overwhelming fetor oris. On this evening severe pain set in along the right brow and the right cheek and in the right inner canthal region. The following morning, July 2, the temperature was normal but there were extensive periorbital edema and severe episcleral injection. Tension of the right eye, taken at this time and again in the afternoon, was normal on both occasions.

30. Sidlick, D. M.: The Use of Solution of Pituitary in Herpes Zoster, Arch. Dermat. & Syph. **22**:91 (July) 1930; cited by Sanford, G. A.: Handbook of Ocular Therapeutics, ed. 2, Philadelphia, Lea & Febiger, 1937.

31. Walker, J. R., and Walker, B. F.: Specific Treatment for Herpes Zoster, Arch. Ophth. **20**:304 (Aug.) 1938.

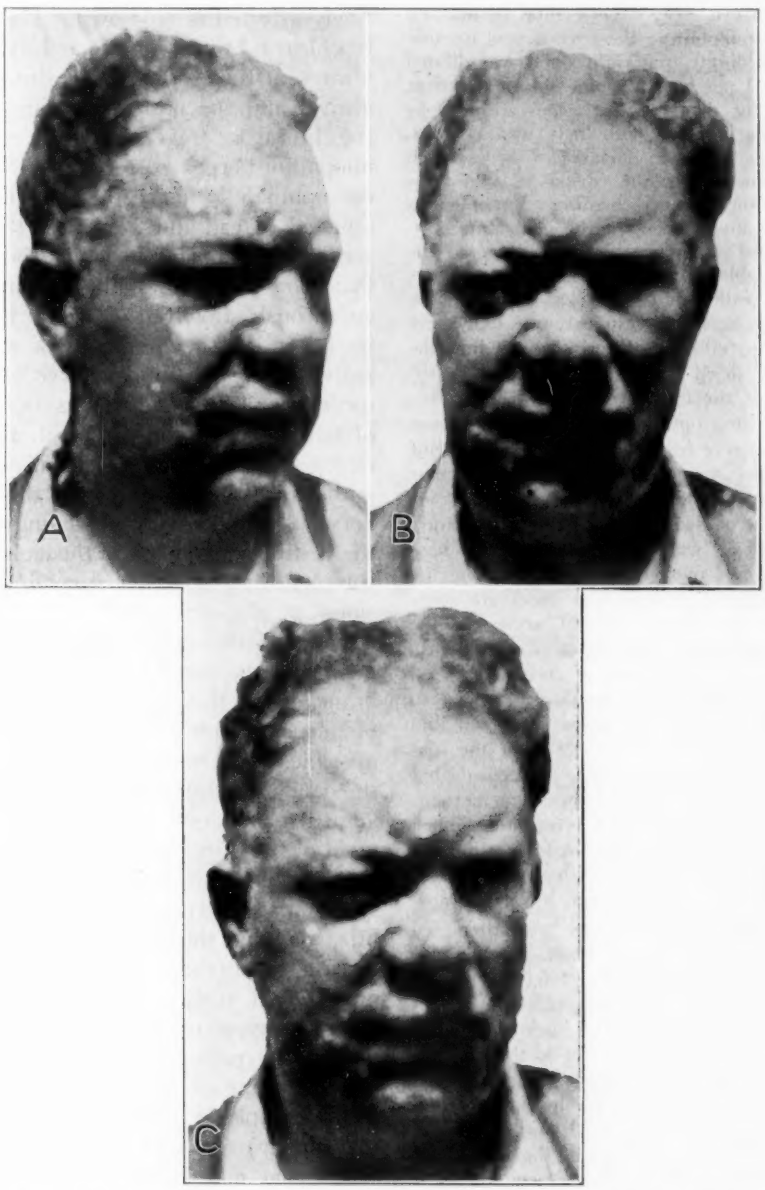
32. Herpes Zoster of the Eye, Bull. Pract. Ophth. **14**:11 (May) 1944.

33. Lillie, W. I.: Treatment of Herpes Zoster Ophthalmicus with Smallpox Vaccine, New York State J. Med. **43**:857 (May 1) 1943.

34. Herpes Simplex of the Eye: Prophylaxis with Use of Cowpox Vaccine, Bull. Pract. Ophth. **13**:27 (Nov.) 1943.

35. Peet, M. M.: Postherpetic Trigeminal Neuralgia, J. A. M. A. **92**:1503 (May 4) 1929.

There was much scleral tenderness, and now the right submaxillary gland was greatly enlarged and hard. Edema was present in the whole right half of the face, and the patient stated that the pain in the lower half of the face, in the roof of the mouth and in the jaw had diminished greatly but that the pain in the supraorbital and supratrochlear regions was more severe than ever. On the following day, July 3, a vesicular eruption appeared on the soft palate, on the tongue and on the right side of the upper lip and on the tip and alar region of the nose. These lesions were too large and atypical to be dismissed as herpes febrilis. Examination of the ear on this day showed edema and a vesicular eruption of the posterior canal wall, with an extremely reddened, but not bulging, tympanum. There was some dental sepsis, and the pharynx was injected. On the



Snapshots of patient with herpes zoster. *A*, herpetic cutaneous lesions involving the ophthalmic branch of the trigeminal nerve (lacrimal, frontal [supraorbital and infratrochlear] and nasociliary), the cutaneous distribution of the right geniculate ganglion and the mandibular branch of the trigeminal nerve, severe submaxillary adenopathy and beginning involvement of the maxillary division of the trigeminus nerve are present. *B*, total efflorescence of herpetiform cutaneous lesions of the ophthalmic, maxillary and mandibular divisions of the trigeminal nerve. Involvement of the nasal tip is pronounced. According to Hutchinson (1866), this means the loss of the eye. Notice the ocular proptosis. *C*, generalized trigeminal cutaneous manifestation of herpes zoster. Preauricular and postauricular adenopathy, periorbital edema and exophthalmos are present. A few lesions involve the distribution of the maxillary division of the left side of the face. This is due to "crossing over" of the fibers of the maxillary division of the right side, a phenomenon which Paton pointed out is not rare in involvement of the ophthalmic division. Interestingly, there was no pain on the left side antecedent to this cutaneous vesiculation due to involvement of the maxillary division of that side.

following day, July 4, a magnificent herpetic eruption was present on the right side of the jaw and of the face, with severe erythema of the right cheek, forehead and right fronto-occipital region. The right side of the upper lip was now greatly swollen and vesicular; the fetor oris was worse, if possible, and the nystagmus and sense of imbalance (due to involvement of the vestibular part of the eighth nerve by connection of the geniculate ganglion with the eighth nerve) had disappeared. The right eye showed periorbital edema and exophthalmos with immobility; the cornea was insensitive to touch. Accordingly, the right pupil was dilated with instillations of 1 per cent atropine sulfate solution. The following day the diagnosis of herpes zoster ophthalmicus et maxillaris et mandibularis was obvious. Not so obvious now was the facial paresis (seventh cranial nerve) on account of the edema and the submaxillary adenitis. The cutaneous manifestation of herpes zoster oticus due to involvement of the geniculate ganglion, however, added one more bizarre feature to the picture in this miserable patient. The cutaneous vesiculation of the whole right side of the face, including the cleft between the face and the right ear, was extremely striking. During the following fifteen days, while the vesiculations slowly dried and scabbed, repeated slit lamp examinations of the eye revealed severe keratitis profunda, while repeated ophthalmoscopic examinations showed an inflamed nerve head with a cloudy posterior chamber. There was a moderate amount of ocular immobility, which could not be accurately tested for magnitude on account of the pain, the patient constantly complaining that his eye "was being pushed out." These ocular findings remained more or less static during the three weeks of disease. There was moderate optic neuritis throughout the illness. Visual acuity in the involved eye one month after the onset of the disease was 20/50. In my previous 6 cases of recent years all therapeutic measures which were employed seemed to be worthless and irrational. Whatever was done did little, if anything, to shorten the duration of the disease; consequently, in the present case it seemed that scrupulous local care of the eye and meeting emergencies, if and when they arose, could promise as much for the patient as a scatter shot attempt at battling the infection (of probable virus origin) with smallpox vaccine, autohemotherapy or convalescent blood therapy.

Consequently, no spectacular therapy was attempted apart from administration of heavy doses of salicylates by mouth, 80 grains (5.2 Gm.) daily, 100,000 units of vitamin A daily by mouth, morphine sulfate hypodermically for pain, atropine sulfate and boric acid ointment to the eye and sulfathiazole powder to the vesicles. At the present writing the patient showed much residual scarring and pitting of the scalp, forehead, nose and face and complained of continuous mild pain, chiefly in the region of the ophthalmic division of the trigeminal nerve and in the roof of the mouth, as sequelae of a condition which was remarkable not only for the extent of the cutaneous nerve involvement but for the severity of localized pain and for the relatively minor involvement of the eye. It did indeed seem that the extent of the ocular involvement was inversely proportional to the severity of the herpetiform cutaneous manifestations.

SUMMARY

Herpes zoster of the trigeminal nerve universally affects the ophthalmic division of that nerve. Antidromic impulses originating in the semilunar ganglion allegedly cause the liberation of histamine-like bodies, which produce the vesicles. Why the ophthalmic branch alone is selectively affected is unknown. The frontal (supratrochlear) branch of the ophthalmic division is always affected, the supraorbital branch nearly always and the nasociliary often. A review of the literature reveals but 1 reported case of idiopathic herpes zoster in which in addition to the ophthalmic nerve the mandibular nerve was affected (Head and Campbell, 1900). Likewise, 1 case was reported in which the ophthalmic and maxillary divisions of the trigeminal nerve were cutaneously involved (Paton, 1926). I found no report in the literature of a case of herpes zoster of the trigeminal nerve in which involvement of all three divisions occurred. A case of more than passing interest, then, to ophthalmologists is herein reported in which, combined with partial herpes zoster of the seventh cranial nerve (Hunt's) and preceding involvement of the vestibular ganglion of the eighth cranial nerve, complete herpes zoster involving all three divisions of the trigeminal nerve occurred. On account of the severe pain, the ocular involvement and the residual scarring on the cutaneous branches of the trigeminal nerve, a diagnosis of herpes simplex or of herpes febrilis is inadmissible. There were displayed in relation to the ocular condition optic neuritis, exophthalmos, keratitis profunda and probable mild involvement of the third, fourth and sixth cranial nerves. No evidence for classifying this case as one of symptomatic herpes zoster arising from encephalitis, syphilis, tuberculosis, leukemia, Hodgkin's disease, hemorrhage in the cerebellopontile angle or cerebral tumor was found. On the other hand, in view of the severe pain and the cutaneous herpetiform manifestations, the case is obviously one of idiopathic herpes zoster of the fifth (complete), seventh (partial) and eighth (vestibular) cranial nerves. All three snapshots reveal the magnificently vesicular efflorescence in various stages of herpetiform cutaneous response to involvement of the geniculate ganglion and of the ophthalmic, maxillary and mandibular divisions of the trigeminal nerve.

2122 North Main Street.

OPHTHALMIC REQUIREMENTS OF THE MILITARY SERVICES

CHANGES FROM JAN. 1, 1944 TO JAN. 1, 1945

CHARLES A. BAHN, M.D.

NEW ORLEANS

At the request of the American Committee on Optics and Visual Physiology, the following supplement is presented. For details, the reader is referred to the original articles.[1]

ARMY, INCLUDING SELECTIVE SERVICE

A. For appointments in commissioned grades, no changes.

B. For induction of enlisted personnel.

Ophthalmologic Requirements According to Classes

Class	1	2	3
Visual acuity 20 ft. (6 m.)	20/20 in each eye	20/40 in each eye, correctable to 20/20, glasses to be worn	20/100 in each eye, correctable to 20/20 and 20/30; glasses to be worn
50 cm.	Jaeger type 1, 50 in each eye	Jaeger type 6 at 50 cm. in each eye, correctable at 50 cm. to Jaeger type 1; glasses to be worn	Jaeger type 1 at 50 cm. and Jaeger type 2 at 50 cm. with correction; glasses to be worn
Depth perception at 6 m.	30 mm. maximum, uncorrected	35 mm. maximum with correction	Pilots only: 40 mm. maximum with correction
Heterophoria			
Esophoria	10 mm. maximum	10 mm. maximum with correction	12 mm. maximum with correction
Exophoria	5 pd maximum	5 pd maximum with correction	7 pd maximum with correction
Hyperphoria	1 pd maximum	1 pd maximum with correction	2 pd maximum with correction
Prism divergence	3-15 pd	3-15 pd with correction	3-15 pd with correction; divergence must equal or exceed esophoria
	Divergence must equal or exceed esophoria		
Field of binocular rotation (red lens test)	No diplopia or suppression within 50 cm. of primary position	No diplopia or suppression within 50 cm. with correction	No diplopia or suppression within 30 cm. with correction
Power of convergence	Pc must not exceed pd *	Pc must not exceed pd * with correction	Omitted
Accommodation	Not less than minimum for age (see table)	OMITTED	

TABLE OF MINIMUM VALUES OF ACCOMMODATION

Age	Diopters	Age	Diopters	Age	Diopters	Age	Diopters	Age	Diopters
17	8.8	23	7.5	29	6.0	35	4.3	41	2.4
18	8.6	24	7.2	30	5.7	36	4.0	42	2.0
19	8.4	25	6.9	31	5.4	37	3.7	43	1.5
20	8.1	26	6.7	32	5.1	38	3.4	44	1.0
21	7.9	27	6.5	33	4.9	39	3.1	45	0.6
22	7.7	28	6.2	34	4.6	40	2.8		

Field of form	Contraction of 15° in any meridian disqualifies (normal limits: temporally, 90°; superiorly, 65°; nasally, 60°; inferiorly, 75°). Disqualifying scotoma: any except physiologic blind-spot on original examination; scotoma due to active process		
Refraction	Maximum: 1.50 D. in any meridian; 0.50 D. of astigmatism	Maximum: 3.00 D. in any meridian; 1.50 D. of astigmatism	No maximum limits

* Pc indicates near convergence point; pd, interpupillary distance.

From the Department of Ophthalmology, Medical Center, Louisiana State University School of Medicine.

1. Bahn, C. A.: Ophthalmic Requirements of the Military Services, Arch. Ophth. **27**:1202-1213 (June) 1942; **29**:831 (May) 1943; **31**:160-161 (Feb.) 1944.

1. General service: (*a*) Binocular (both eyes open) vision of not less than 20/40 without glasses, provided the vision in the more defective eye is not less than 20/70 without glasses and provided the defective vision is not due to active or progressive organic disease.

   (*b*) Visual acuity without glasses of not less than 20/200 in each eye, provided vision is correctable to 20/40 in each eye and provided the defective vision is not due to active or progressive organic disease. The actual possession of suitable glasses by an individual is not required for his acceptance under these standards.[2]

2. Limited service: (*a*) Minimum vision of 20/400 in each eye without glasses, correctable to 20/40 in one eye and 20/70 in the other eye, or 20/30 in one eye and 20/100 in the other eye.

   (*b*) Loss of one eye (anophthalmos) or any degree of defective vision in one eye from 20/400 to absence of light perception, if such defective vision is not due to active or progressive organic disease, with vision in the other eye of 20/100 without glasses, correctable to 20/20 with glasses.

C. Air Corps: Flying.

2. Effective only from April 1944 to September 1944: general service: Visual acuity without glasses of not less than 20/200 in each eye or 20/100 in one eye and 20/400 in the second eye, provided vision is correctable to 20/40 in each eye, to 20/30 in one eye and 20/70 in the other eye or to 20/20 in one eye and 20/400 in the other eye, and provided the defective vision is not due to active or progressive organic disease. The actual possession of suitable glasses by a candidate is not required for his acceptance under these standards.

NAVY; MARINE CORPS; MERCHANT MARINE; COAST GUARD, AND UNITED STATES PUBLIC HEALTH SERVICE

No changes have been made. For requirements, see original articles.[1]

The committee acknowledges the cooperation and assistance of Surgeon General Norman T. Kirk and Lieutenant Colonel G. E. Gorman, of the United States Army; Surgeon General Ross T. McIntire, of the United States Navy, and Surgeon General Thomas Parran, of the United States Public Health Service.

The regulations supplementing the bibliography given in the original articles are contained in the following authorities:

Letter from Surgeon General of the Army, Jan. 26, 1945.

Letter from Surgeon General of the Navy, Jan. 9, 1945,

Letter from Surgeon General, United States Public Health Service, Feb. 8, 1945.

1028 Maison Blanche Building.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Bacteriology and Serology

RELATIONSHIP BETWEEN THE BACTERIOLOGY OF THE CONJUNCTIVA AND NASAL MUCOSA. C. BERENS and E. L. NILSON, Am. J. Ophth. **27:** 747 (July) 1944.

Berens and Nilson found that 50 per cent of the 83 sets of cultures of material taken from the nasal and conjunctival membranes of 75 patients with extraocular diseases yielded organisms similar in type and toxicity for both the conjunctival and the corresponding nasal membranes, 43.3 per cent yielded "toxic" organisms in cultures of nasal secretions, with corresponding "negative" cultures of conjunctival material and approximately 3.5 per cent yielded organisms of slightly greater toxicity in cultures from the eye than in those from the nose.

In determining the etiologic factors of chronic and recurrent extraocular inflammatory diseases, it is advisable to investigate the nasal mucosa as a possible source of infection.

W. S. REESE.

Biochemistry

THE METABOLISM OF THE CORNEA. O. S. LEE, JR. and W. M. HART, Am. J. Ophth. **27:** 488 (May) 1944.

Lee and Hart give the following summary of their work:

"1. The normal epithelium of the cornea is shown to have a high oxygen uptake in contrast to a low uptake by the stroma. Because the endothelium consists of only a single layer of cells, it was impossible to measure its oxygen consumption by this method.

"2. The oxygen uptake of the corneal epithelium of riboflavin-deficient rats was found to be lessened. This may be accounted for by the cellular necrosis present in the epithelial cells of such corneas. When vascularization was present, the oxygen uptake by the stroma was found to be elevated, whereas in the absence of vascularization the oxygen uptake remained low. It is reasonable to assume that the increased oxygen uptake by the stroma is the result of vascularization and cellular infiltration.

"3. The metabolic activity of the xerotic cornea was found to be normal or higher than normal. The presence of metaplasia and hyperplasia instead of an actual cellular destruction of the corneal epithelium may be responsible for the approximately normal oxygen consumption of corneas of rats with vitamin-A deficiency."

W. S. REESE.

Conjunctiva

SYPHILIS OF THE CONJUNCTIVA. J. L. CASTILLO, Arch. de oftal. de Buenos Aires **18:** 165 (March) 1943.

Syphilis of the conjunctiva is rare. It may appear as a chancre, as simple conjunctivitis, as scleroconjunctival infiltration and pseudotrachoma of the tarsal conjunctiva and as gumma of the eyeball. There are no references in the literature to hereditary syphilis of the conjunctiva. A girl aged 10 years had subacute inflammation and infiltration of the cornea, which simulated tuberculosis. The Kahn reaction for syphilis was negative. The Mantoux test with a 1:1,000 dilution was strongly positive for tuberculosis. Antituberculosis treatment failed. Antisyphilitic therapy was administered because of the moderate hepatomegaly and splenomegaly, mild diffuse adenopathy and a high palate. The Kahn and Kline reactions became weakly positive in the course of antisyphilitic therapy. Rapid improvement and cure of the conjunctiva followed. The condition was diagnosed as hereditary syphilis of the conjunctiva.

J. A. M. A. (W. ZENTMAYER)

Cornea and Sclera

VITREOUS STRIAE AND RETROCORNEAL TRABECULAE FOLLOWING INTERSTITIAL KERATITIS. L. SÁNCHEZ BULNES, Arch. Asoc. para evit. ceguera México **1:** 81, 1942.

A woman aged 35, who had interstitial keratitis thirty years before, presented a V-shaped formation of corneal-vitreous striae and retrocorneal trabeculae with oblique illumination. Visual acuity was 6/10 in the right eye and 3/10 in the left eye.

The first description of these striae was given by Raehlmann, in 1877, and by Fridenberg, in 1895. Fridenberg stated that they were deposits of fat in the lymphatic spaces of the cornea.

Such vitreous striae may be adherent to the posterior corneal surface or may bridge out as trabeculae into the anterior chamber, fixed at either end to Descemet's membrane, and they occur in all types of interstitial keratitis. They must be differentiated from folds in Descemet's membrane.

Several hypotheses have been advanced to explain their formation:

(1) Cicatricial retraction of the corneal parenchyma takes place during the period of healing of the keratitis, forcing Descemet's membrane into folds into the anterior chamber; (2) the striae are residuals of a plastic inflammatory

process in the anterior chamber, and (3) folds of endothelial cells separate from Descemet's membrane and then secrete a vitreous substance, similar to that of the vitreous membrane. Later the two layers of the fold unite to form a retrocorneal tube, and under the cicatricial traction of the cornea partially separate from the posterior surface to form the trabeculae in the anterior chamber.

H. F. CARRASQUILLO.

Experimental Pathology

EFFECT OF CHEMOTHERAPEUTIC AGENTS ON CELL DIVISION AND HEALING OF CORNEAL BURNS AND ABRASIONS IN THE RAT. G. K. SMELSER and V. OZANICS, Am. J. Ophth. **27:** 1063 (Oct.) 1944.

Smelzer and Ozanics give the following summary:

"1. Extensive corneal abrasions healed without a marked increase in the number of mitotic figures.

"2. Thermal burns became covered with epithelium in about the same length of time as did abrasions (12-18 hours), but a great increase in the number of mitotic figures was found during this procedure.

"3. Sulfacetimide, sulfapyrazine, and penicillin applied as ointments, powders or solutions had no effect on cell division in the intact rat cornea.

"4. Sulfadiazine tended to increase cell division and sulfathiazole to depress mitosis in this epithelium.

"5. Sulfonamides and penicillin, in general, had no deleterious effect on cell division in abraded corneas, although the number of mitoses was low in over half of the sulfathiazole-treated animals.

"6. Sulfonamides and penicillin did not interfere with cell division in burned corneal epithelium.

"7. Sulfathiazole and sulfacetimide inhibited cell migration following corneal burns, whereas sulfadiazine and penicillin were but slightly detrimental.

"8. Sulfonamide ointments inhibited cell migration slightly less than did powders.

"9. It is realized that these results are qualified by the form of administration and the relative ability of the compounds to penetrate the cornea."

W. S. REESE.

General Pathology

OCULAR PATHOLOGY IN VARIOUS TYPES OF DIETARY DEFICIENCIES, WITH PARTICULAR EMPHASIS ON ARTERIOLAR SCLEROSIS: EXPERIMENTAL STUDY. A. A. KNAPP and S. N. BLACKBERG, U. S. Nav. M. Bull. **41:** 1339 (Sept.) 1943.

Knapp and Blackberg report that lesions resembling senile arteriolosclerosis in man were produced in the eyes of rats with various types of malnutrition. Faulty nutrition, irrespective of whether the deficiency was caused by inadequate caloric intake or by lack of vitamin A or the vitamin B complex, consistently produced an increased light reflex, pallor and uniform attenuation of the arterioles along their entire course. In previous experiments the authors observed that similar pathologic changes were associated with vitamin D deficiency. The arteriosclerosis induced was not specific for any vitamin deficiency but followed a general, nonspecific disturbance of the cellular nutrition.

J. A. M. A. (W. ZENTMAYER)

Glaucoma

THE MACULA-WEDGE SCOTOMA: A PROGNOSTIC INDEX IN GLAUCOMA. J. N. EVANS, Am. J. Ophth. **27:** 1090 (Oct.) 1944.

After a brief discussion of central field defects associated with glaucoma, Evans describes a new defect which he designates as "macula-wedge" scotoma. It is triangular, and its base arises from the concave border of the sickle defect (scimitar, or Bjerrum defect), and its apex points toward the fixation point.

W. S. REESE.

Hygiene, Sociology, Education and History

INDUSTRIAL EYE HEALTH PROBLEMS. H. S. KUHN, Am. J. Pub. Health **33:** 1103 (Sept.) 1943.

Two problems are of concern to both management and employees: the need of a standard visual test on admission and the use of a similar visual testing procedure in conducting a survey of employees within a given industry. Visual testing falls into three main categories: preemployment examination, periodic rechecks of special groups and the plant survey. Special emphasis on tests for near vision is always indicated when an employee is 40 years and over. The various rehabilitation problems involved in a war program are becoming increasingly important. Among these corrective problems are training of adults who lack coordination of the ocular muscles in development of the needed binocular skills; proper refraction for the distance required by the job and prescription of glasses in relation to that job; detection and care of changes in or disease of an employee's eyes as revealed in the periodic testing, and equipment of each employee so that he is able to meet the visual requirements of his assigned job. Progress in the field of industrial ophthalmology, in eye protection equipment, in the analysis of visual aptitudes, in the classification of jobs as related to visual skills and, especially, in the unexpected responsibilities of ocular rehabilitation in a country at war has been so rapid that constant reference to current scientific literature is indicated.

W. ZENTMAYER.

Injuries

PNEUMO-ENCEPHALOCELE, SECONDARY TO A PUNCTURE WOUND OF THE LID. H. SLAUGHTER and B. Y. ALVIS, Am. J. Ophth. **27:** 617 (June) 1944.

The case of a child who presumably injured her lid with a pencil is described. Pus was obtained when the lid was incised, culture of which showed Staphylococcus aureus. A diagnosis of traumatic pneumoencephalocele was made on the basis of the roentgenogram. The child recovered.

W. S. REESE.

ACTINIC KERATOCONJUNCTIVITIS. R. G. SCOBEE and E. W. GRIFFEY, Am. J. Ophth. **27:** 632 (June) 1944.

Scobee and Griffey conclude that actinic keratoconjunctivitis, or "flash burn," is an important industrial disease and that the causative agent is ultraviolet irradiation. Epinephrine used early greatly reduces the severity, or even aborts the condition entirely.

W. S. REESE.

SOVIET MILITARY OPHTHALMOLOGY. A. A. KOLEN, Lancet **1:** 804-805 (June 26) 1943.

Soviet ophthalmologists have paid a great deal of attention to the study of war injuries of the eyes, and the military ophthalmic services are so equipped as to insure the earliest possible skilled attention to the wounded eyes. This article speaks of the following plastic procedures: reconstruction of the conjunctival sac, correction of contracted scars and reconstruction of an eyelid by the flap method of Kurloff. Plastic operations are performed within two to four months after the injury, so as to facilitate early rehabilitation of the patient. To facilitate the disappearance of unsightly scars, paraffin therapy is practiced. In cases of prolapse of the ciliary body associated with scleral rupture of the eyeball the Soviet surgeons do not hesitate to excise the prolapsed ciliary body and then unite the scleral wound with sutures; in fact, they speak of surgery of the ciliary body.

Transfusions are widely used in the treatment of ocular wounds. They are regarded as especially useful in cases of traumatic opacities of the vitreous, traumatic iridocyclitis and threatened sympathetic ophthalmia. In an injury of the ciliary body a prophylactic transfusion of 150 to 200 cc. of blood is made. Absorption of the opacities in the vitreous has been facilitated by transfusion into the duodenum by means of the duodenal probe of between 50 and 120 cc. of duodenal juice. Blood transfusion is combined with paracentesis of the anterior chamber in cases of severe and persistent vitreous opacities. With infected injuries of the eyeball excellent results have been achieved by the administration of sulfacetimide, and the advantages of vitamin K in prevention of threatened hemorrhages are mentioned.

This brief and somewhat optimistic article will be found stimulating and suggestive.

ARNOLD KNAPP.

Lacrimal Apparatus

THE LACRIMATION REFLEX. J. R. MUTCH, Brit. J. Ophth. **28:** 318 (July) 1944.

Mutch, in this lengthy article, considers the lacrimation reflex under the headings of physiology, nerve supply, experimental observations, clinical observations and conclusions. He draws the following conclusions:

Reflex lacrimation is unilateral and can be inhibited by surface anesthesia of the conjunctiva and cornea and by section or paralysis of the ophthalmic division of the fifth cranial nerve. This nerve is therefore the sensory, or afferent, pathway for reflex lacrimation.

The efferent pathway runs in the seventh cranial nerve but is independent of the motor fibers to the facial muscles (syndrome of crocodile tears) and of the seventh nerve in the brain near the nucleus of the sixth nerve (Foville's syndrome, or lateral gaze paralysis) and is also peripheral to the geniculate ganglion (Bell's palsy, with loss of taste on the anterior two thirds of the tongue).

If the greater superficial petrosal nerve is cut or the sphenopalatine ganglion is blocked, no reflex or psychic lacrimation takes place, even though the ophthalmic division of the fifth nerve is left intact, while psychic lacrimation is normal if the sensory root of the fifth nerve is cut and the greater superficial petrosal nerve is spared. Motor impulses must therefore pass along the greater superficial petrosal nerve.

Psychic weeping is bilateral and cannot be inhibited by surface anesthesia or paralysis of the fifth cranial nerve or by section of the cervical sympathetic nerve.

On anatomic grounds, it is assumed that the fibers from the sphenopalatine ganglion which enter the maxillary nerve run to the trigeminal (gasserian) ganglion before they pass along the zygomatic nerve.

No interference with reflex or psychic lacrimation results from either unilateral or bilateral section of the cervical sympathetic chain in the neck. One patient did complain that her eyes felt unduly dry toward night; so there is a possibility that mucus from the glands in the conjunctiva may be inhibited. On no occasion, however, has keratitis sicca been observed in any patient who has had a sympathectomy. It is unlikely, therefore, that the sympathetic nerve takes any part in reflex or psychic lacrimation.

W. ZENTMAYER.

Lens

A Report on a Family with Ectopic Lenses. C. A. Clapp, Am. J. Ophth. **27:** 738 (July) 1944.

Clapp reports on 11 children in one family of whom 8 have misplaced lenses and a ninth has congenital cataract.

W. S. Reese.

Corneal Sutures in Cataract Operation. L. E. Martínez, Arch. Asoc. para evit. ceguera México **1:** 155, 1942.

The author states that although good results have been obtained with the classic cataract operation in a large percentage of cases since Daviel's time, the use of sutures to avoid postoperative complications has become established. Sutures are most useful in intracapsular extraction, with which loss of vitreous is more likely to occur.

The following types of suture are used: conjunctivocorneal, corneoscleral intracorneoscleral and suture by layers. The first type has been described by Arganaraz of Buenos Aires. As an example of the corneoscleral type, the author cites the suture devised by Liégard, modifications of which have been described by Olmos, Chavira and Torres Estrada. The suture described by Suárez de Mendoza is of the intracorneoscleral type, and Castroviejo employs suture by layers.

The author explains the procedure employed with each type of suture. He is of the opinion that the use of sutures is an advance in ophthalmology and states that even if all complications cannot be avoided, they should nevertheless be employed systematically.

H. F. Carrasquillo.

Methods of Examination

Ocular Biophotomicrography: Preliminary Report. M. de Rivas Cherif, Arch. Asoc. para evit. ceguera México **1:** 119, 1942.

It is the author's belief, although he has not yet reviewed the literature, that attempts must have been made to obtain photomicrographs of the living eye, but with no practical results, since he has never seen such pictures in publications of any kind. He has succeeded in obtaining biophotomicrographs of the eye, which, although not perfect at present, he hopes to improve on so that they will be of practical value.

He employs a camera obscura without an objective of its own, utilizing the oculars of the biomicroscope. As the corneal microscope is binocular, he uses one of the oculars for observation and the other for photography. He describes and illustrates the simple apparatus which he employs in the experimental work and shows some of the photographs obtained.

H. F. Carrasquillo.

Neurology

A Diffuse Neurofibromatosis of the Bulbar Conjunctiva (Recklinghausen's Disease), with Lesions of the Osseous System and of the Skin, Bodily Asymmetry and Intracranial Disturbances: Report of a Case. F. P. Allende, Arch de oftal. de Buenos Aires **18:** 438 (Sept.) 1943.

The author discusses Recklinghausen's disease. He establishes three clinical groups: cases in which the invasion of the central nervous system is predominant; cases in which the cutaneous lesions are the principal manifestation of the disease, and cases in which involvement of the skeletal system is predominant.

When the structures of the eye are involved, the order of preference is as follows: first the lids and optic nerve; then the orbit, retina, choroid, iris, cornea and tarsal conjunctiva, and, last, the bulbar conjunctiva. The author describes the different types of lesions in these locations and stresses the rarity of involvement of the bulbar conjunctiva. He refers to the fact that Duke-Elder mentions only 2 cases so far described, that after careful search of the literature he himself found reports of only 3 cases and that from 1932 to 1942 articles containing only 34 cases of the disease with ocular complications are listed in the *Quarterly Cumulative Index Medicus.*

He reports a case with involvement of the bulbar conjunctiva in a girl aged 18. General physical examination showed developmental asymmetry of the body, with predominance of the right side; two large patches of baldness over the right temporoparietal region, with a solid tumor, the size of a hazelnut, in the temporal region, and typical café au lait macular lesions of the skin. Neurologic examination revealed that the patient was epileptic, and a psychiatric study demonstrated that she was mentally retarded when going to school.

Right Eye.—Examination revealed hyperplasia of the surface of the skin adjacent to the temporal region; cranio-orbital asymmetry; a pinkish, hair-free tumor in the superciliary region; a smaller growth over the anterior surface of the upper lid; blepharoptosis; hypertrophy of the palpebral portion of the lacrimal gland; a flat, round tumor in the bulbar conjunctiva near the limbus at 3 o'clock; a small tumor in the caruncle, and a larger tumor in the bulbar conjunctiva, above the cornea and slightly invading it, which measured 2 cm. in its widest dimension. Examination of the fundus revealed the presence of a fine, epipapillary membrane. The rest of the fundus was normal. Vision was 1/6 and was not improved by glasses or pinhole disk.

The left eye was normal.

Laboratory examination revealed essentially nothing abnormal. Roentgenographic studies con-

firmed the cranio-orbital and bodily asymmetry. Biopsy confirmed the diagnosis of neurofibromatosis.

The article is well illustrated with photographs and photomicrographs.

H. F. CARRASQUILLO.

Ocular Muscles

PHENOMENA ASSOCIATED WITH ECCENTRIC FIXATION. G. GUIBOR, Am. J. Ophth. **27:** 986 (Sept.) 1944.

Guibor gives the following summary:

"The phenomena associated with eccentric fixation when studied intensively may be summarized under three headings: 1. Disturbances associated with the motor apparatus. 2. Disturbances associated with the visual apparatus. 3. Disturbances associated with the proprioceptive apparatus.

"Disturbances associated with the motor apparatus may be said to be: 1. The esotropia. 2. The limitation of abduction (weakness in the left external rectus muscle). Induced homonymous diplopia which increased in the field of the left external rectus muscle. 3. Abnormal electroencephalogram.

"Disturbances associated with the visual apparatus may be outlined as: 1. Amblyopia (3/200: 3/140). 2. A central scotoma. 3. Normal peripheral field. 4. Normal projection. 5. Abnormal correspondence.

"Disturbances associated with the proprioceptive apparatus may be said to be illustrated by: 1. Head rotation. 2. Past pointing. 3. Past walking.

"Note: Authorities do not agree that a proprioceptive apparatus is present in the extraocular-motor mechanism. Clinical evidence suggests that such a mechanism does exist."

W. S. REESE.

Pharmacology

REACTIVITY OF THE OCULAR TISSUES TO WETTING AGENTS. K. C. SWAN, Am. J. Ophth. **27:** 1118 (Oct.) 1944.

Swan points out that although the low toxicity of wetting agents has been stressed in the literature and in commercial advertisements, these surface-active compounds are capable of producing reactions in ocular tissues; indeed, minute amounts injected into the anterior chamber produce violent reactions.

W. S. REESE.

SOME NEW CHOLINE ESTERS WITH CYCLOPLEGIC AND MYDRIATIC ACTION. K. C. SWAN and N. G. WHITE, Proc. Soc. Exper. Biol. & Med. **53:** 164 (June) 1943.

Choline derivatives, such as acetylcholine and carbaminoylcholine, are miotics and cyclotonics. The authors have synthesized new choline esters by substituting highly hydrophobic groups for the acetyl radical in acetylcholine. The resulting elongated molecules have proved highly surface active, in sharp contrast to the surface-inactive acetylcholine. Of the new compounds, di-n-butylcarbaminoylcholine sulfate has been found to be a powerful mydriatic and cycloplegic. Two instillations of a 7.5 per cent solution of the compound into the conjunctival sac of an adult patient produce mydriasis and cycloplegia, beginning within twenty minutes and becoming maximal in sixty to ninety minutes. The reactions of the intrinsic muscles usually return to normal seven to twelve hours after administration. Four hundred patients received two instillations of 5 per cent homatropine hydrobromide in one eye and two instillations of a 7.5 per cent solution of the new drug in the other. There was little difference in the degree of mydriasis and cycloplegia produced by the two drugs; however, cycloplegia, and particularly mydriasis, was shorter after the administration of the new drug. Synthesis and pharmacologic investigation of surface-active choline esters are being continued.

KRONFELD.

Refraction and Accommodation

"BIASTIGMATISM." A. LINKSZ and W. TRILLER, Am. J. Ophth. **27:** 992 (Sept.) 1944.

Linksz and Triller conclude from their studies that since the Márquez procedure cannot furnish more accurate results than the direct use of the astigmatic dial there is nothing that would recommend the adoption of this complicated technic for routine refractive examinations.

W. S. REESE.

THE GAS MASK WAFER FOR PRESBYOPIA. W. O. G. TAYLOR, Brit. J. Ophth. **28:** 461 (Sept.) 1944.

Taylor describes a method of correction of presbyopia for use on respirators with or without additional correction for ametropia. The optical problems are considered. The device has the advantage of cheapness, lightness, absence of mechanical parts, freedom from dimming and ease of testing and fitting. The article is illustrated.

W. ZENTMAYER.

Retina and Optic Nerve

ARTERIOLAR THROMBOSIS OF THE RETINA. C. S. DAMEL and M. BRODSKY, Arch. de oftal. de Buenos Aires **18:** 429 (Sept.) 1943.

The authors report the case of an athlete aged 33 who had been alcoholic all his life. The Wassermann and Kahn reactions of the blood were negative. One month before the visual symptoms appeared he began to lose weight and strength, and ten days after this he had a cerebral episode, with loss of consciousness for eight

hours. Twenty days later he complained of blurred vision in the right eye.

Visual acuity was 4/10 in the right eye and 8/10 in the left eye. External examination revealed nothing abnormal in either eye, and the ophthalmoscopic findings in the left eye were normal. In the right eye there were arteriosclerotic changes in the inferior macular artery, a branch of which was completely obliterated with a resulting edematous area having an elevation of 4 D. in the region of the macula. Numerous white dots were also seen in this zone.

Study of the fields in this eye demonstrated a triangular sector defect, limited by a straight line continuous with a scotoma surrounding the central area, which was free. Eight months later vision in the right eye was 8/10, and the edematous area at the macular was attenuated. The visual field remained unchanged.

The authors differentiate the condition from embolism, endarteritis and thrombosis, toxic and diffused periarteritis and local ischemic states brought about by orbital conditions, the result of traumatism, pressure and inflammatory processes. They state that their case falls into the category of the condition described by Friedenwald as "retinal arteriolar thrombosis."

The article is illustrated.

H. F. CARRASQUILLO.

Tumors

OCULAR COMPLICATIONS OF TUMORS OF THE NASOPHARYNX. B. J. TISCORNIA and I. LAMI, Arch. de oftal. de Buenos Aires **18:** 557 (Nov.) 1943.

Little has been written in ophthalmologic literature on this subject, although the condition frequently produces initial ocular symptoms.

After the authors describe the intranasal and extranasal symptoms of the disorder, they mention the following ocular manifestations: muscular palsies, enophthalmos, neuralgias, ptosis, exophthalmos, edema and atrophy of the optic nerve, which, according to many observers, are common in the disease.

The anatomy of the nasopharynx and the surrounding region is described in detail, and how involvement of the different nerve structures is responsible for the ocular manifestations. The extension to the external rectus muscle occurs early at times, and paralytic convergent squint is the result. The third nerve is usually invaded late in the disease, producing external or internal ophthalmoplegia. The optic nerve may be involved, and papilledema or atrophy may occur.

Involvement of the gasserian ganglion may result in severe neuralgia. Horner's syndrome may occur from involvement of the ciliospinal center or the cervical sympathetic outflow, and unilateral miosis, ptosis, ocular hypotony, exophthalmos and congestion of the skin of the side of the face may be noted.

Exophthalmos is frequent and is the result of invasion of the orbit by the tumor. Abnormality in the lacrimal secretion may be produced by involvement of the secretory branches of the facial nerve.

The most common tumors involving the nasopharynx are the epitheliomas and the sarcomas. Observations in 8 clinical cases are given.

H. F. CARRASQUILLO.

Uvea

A CASE OF CORPORA NIGRA WITH ANTERIOR SYNECHIA. R. CRAWFORD, Brit. J. Ophth. **28:** 410 (Aug.) 1944.

The especial feature of the case was the attachment of one of the upper corpora nigra in the left eye to the back of the cornea over a flattened area of about 2 mm. The position and size remained constant whether the pupil was normal or dilated. It is suggested that one of the flocculi passed through the pupillary membrane about the fifth month of fetal life, when the marginal sinus is well developed and the anterior chamber is still shallow, and became adherent to the cornea.

W. ZENTMAYER.

Vision

THE DISSOCIATION OF FORM VISION AND LIGHT PERCEPTION IN STRABISMIC AMBLYOPIA. G. WALD and H. M. BURIAN, Am. J. Ophth. **27:** 950 (Sept.) 1944.

Wald and Burian give the following summary:

"1. The absolute threshold of vision has been measured under various circumstances in five patients with strabismic amblyopia. In all cases thresholds were determined alternately in the amblyopic and dominant eyes. Three types of measurement were performed: (*a*) dark adaptation following a high state of light adaptation; (*b*) the distribution of thresholds over the retinal surface, central and peripheral, in the dark-adapted eye; and (*c*) the variation of threshold with wave length, centrally and peripherally, in the dark-adapted eye.

"2. In all cases the threshold of the amblyopic eye was found to be essentially normal, foveally and peripherally, in cones and rods, and in light and dark adaptation. With this is associated a capacity approaching normal for fixating and localizing illuminated points and areas on the central and peripheral retina.

"3. The entire apparatus of simple light perception and spatial localization within the visual field is therefore virtually normal in these patients. Since, however, the visual acuities of their amblyopic eyes were in no case higher than 20/200, the apparatus of pattern vision must be to some degree distinct from that which mediates the other visual functions.

"4. Subhuman mammals which have been deprived of the occipital lobes of the cerebral cortex, which contain the visual areas, also lose virtually all capacity for pattern vision while retaining sensitivity to light, brightness discrimination, and visual-space localization. Pattern vision in mammals generally, therefore, requires the cortex, while other visual functions appear to be in large measure subcortical. In man there is evidence that all sensory aspects of vision have indispensable cortical components. Our experiments, however, show that here also some degree of anatomic dissociation of visual functions must exist.

"5. In view of these relationships, and of the demonstrated effectiveness of use and training in curing some cases of strabismic amblyopia, it is concluded that this disability consists in a cortical inhibition of the higher cortical function of pattern vision without notable impairment of the lower cortical functions of light perception and spatial projection.

"6. The possibility exists that this inhibition involves principally the macular projection on the cortex and, perhaps as a consequence of this, pattern vision primarily in bright light."

W. S. REESE.

NIGHT BLINDNESS OF WAR. P. H. WOSIKA, War Med. **4:** 331 (Sept.) 1943.

According to Wosika, night blindness of war was first reported during the Crusades, and since that time almost all major military efforts have been accompanied with night blindness, particularly wherever overstraining, heat, sun blinding, hunger and thirst have occurred. The First World War was responsible for much literature on this subject. The term "night blindness of war" embraces organic and idiopathic night blindness. In the literature poor dark adaptation, as measured by instruments, also has been included under this term. Malnutrition (lack of vitamin A) causes night blindness, xerosis and xerophthalmia. Therapeutic correction is simple, swift and sure. Poor dark adaptation does not seem related to night blindness, xerosis, xerophthalmia or food inadequacy. Therapeutic correction is not successful, even with huge supplemental doses of vitamin A. In the present state of knowledge of scotopic vision, night blindness and poor adaptation must be differentiated. It is suggested that further work with the rate and end values of dark adaptation concerning rods, cones and influences of the nervous system be performed in an attempt to establish a firm physiologic basis for dark adaptation tests. While dark adaptation tests do measure the ability to see in low luminosity, the controlling mechanism is not established; the relation to vitamin A is not clear, and its usefulness in military medicine as regards night blindness of war must be questioned, although further refinements of technic may enhance the value of the test.

J. A. M. A. (W. ZENTMAYER)

Therapeutics

VITAMINS IN OPHTHALMOLOGY. I. BILGER, Göz. klin. **1:** 43, 1943.

The author states that when one surveys the advances made in the study of nutrition up to the present, one is impressed with the importance of the vitamins. With respect to the ocular disorders, the absence of vitamin A causes day blindness, xerophthalmia and keratomalacia and secondarily is concerned with lesions of the cornea, lids and conjunctiva and with strabismus.

W. ZENTMAYER.

News and Notes

EDITED BY W. L. BENEDICT

GENERAL NEWS

Ophthalmologic Seminar, Emory University School of Medicine.—The ophthalmologic seminar announced by Emory University School of Medicine has been postponed on advice from the War Committee on Conventions.

American Orthoptic Council: Examinations for Technicians.—The next examination by the American Orthoptic Council will be held in September and October 1945.

The written examinations will be held at various cities in the country on Friday, September 7. Only candidates passing the written examinations will be permitted to take the oral and practical tests, to be given in Chicago, Saturday, October 6.

Applications on official forms must be received before July 1, 1945.

Address: The American Orthoptic Council, 23 East Seventy-Ninth Street, New York 21.

Society Transactions

EDITED BY DR. W. L. BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

THOMAS H. JOHNSON, M.D., *Chairman*
AND
WENDELL L. HUGHES, M.D., *Secretary*

Regular Meeting, Nov. 20, 1944

Choroideremia: Report of a Case. DR. HARRY MAGDER, Kirkland Lake, Ontario, Canada (by invitation).

A case of choroideremia in a man aged 58 is presented. The patient was only slightly myopic, whereas most patients reported on have shown a moderate or high degree of myopia.

The disease had been progressive for over ten years, so that a change from night work to day work was necessary three years ago. The fundus picture and field defects were practically identical in the two eyes. Central visual acuity has remained fairly good, despite the advanced condition of the disease.

DISCUSSION

DR. W. GUERNSEY FREY: In the twenty-two years during which I have been associated with various eye and ear hospitals in Brooklyn, Queens and Manhattan, this is the first case of choroideremia I have knowingly encountered. The only diagnosis with which this condition might be confused is retinitis pigmentosa, and the resemblance there is only with respect to night blindness, not appearance.

DR. JOSEPH ANTHONY SCHULTZ, Buffalo: Were any choroidal vessels at all observed?

DR. HARRY MAGDER, Kirkland Lakes, Ontario, Canada: Yes, in the periphery of each eye considerable choroidal tissue was to be seen, with the vessels as well.

Ophthalmic Features of Intracranial Chordoma and Allied Tumors of the Clivus. DR. ISADORE GIVNER.

This paper will be published in full in a future issue of the ARCHIVES.

Effect of Local Anesthetics on Healing of Burns of the Cornea. DR. G. K. SMELSER.

The effects of local anesthetics on two major factors in the healing of epithelial injuries, mitosis and migration of the cells, are compared. Seven anesthetics (cocaine, 0.5 per cent; tetracaine hydrochloride, 0.5, 0.25 and 0.1 per cent; phenacaine hydrochloride, 2 and 0.5 per cent; butacaine sulfate, 2 and 0.5 per cent; butesin picrate, 0.75 and 2 per cent, and orthoform, 2 per cent) were studied. These concentrations are those which are clinically useful. These compounds were applied as aqueous solutions, or as ointments or as both. An ointment base and an aqueous solution of hydrogen ion concentration similar to that of the anesthetic solutions were tested in like manner.

Young male rats of the Sherman strain were used. Standard thermal burns were made on each eye with a special Shahan thermophore, as described in earlier reports. Untreated burns were covered with epithelium in twelve to fifteen hours. The control series showed that the speed of migration and the number of mitotic figures were essentially the same in the two eyes. The substances to be tested were placed on the right eye for one minute every two hours. Autopsy was performed on the animal twelve hours after the injury, and the eyes were fixed. Camera lucida drawings were made of the portion of the burn which remained uncovered by epithelium, and the area thus outlined was measured with a planimeter. Counts of the mitotic figures in the regenerating epithelium were made from paraffin sections. The effect of the anesthetic was judged by comparing the treated eye with the untreated, control, left eye of the same animal.

The effect of these anesthetics on mitosis in the intact cornea is reported. When the same drug at the same concentration is applied to an injured eye its inhibitory effect on cell division is often greater than in the intact eye. This is due, perhaps, to the greater ability of the drug to enter broken epithelium. In these experiments all the anesthetics checked cell division appreciably except for phenacaine hydrochloride, 0.5 per cent, and butesin picrate 0.75 per cent. The form in which the drug was administered was also important, for an ointment containing butacaine sulfate in 2 per cent concentration was much less inhibitory than the same drug in a 2 per cent solution.

All substances tested retarded migration of the epithelial cells over the burned area. A control solution (boric acid, p_H 4.0) and anhydrous wool fat, the ointment base, slightly inhibited cell migration. Solutions of nupercaine hydrochloride, 0.25 per cent; butacaine sulfate, 2 per cent, and tetracaine hydrochloride, 0.5 per cent, and phenacaine hydrochloride, 2 per cent, notably restricted cell movement. Some of the anesthetics actually enlarged the denuded area, possibly because of their detergent qualities. However, certain anesthetics in low concentrations are relatively harmless to regenerating epithelium. Solutions of phenacaine hydrochloride, 0.5 per cent, or cocaine, 0.5 per cent, and ointments contain-

ing butacaine sulfate, 2 per cent, or butesin picrate, 0.75 per cent, did not notably delay healing as compared with an ointment with an anhydrous wool fat base or a 3 per cent solution of boric acid.

DISCUSSION

DR. CHARLES ALLEN PERERA: I should like to ask Dr. Smelser whether there is any way to differentiate between the local chemical effect of the anesthetic on the epithelium and the trophic effect of anesthesia of the corneal nerves on the growth of epithelium, and whether there would be any point in carrying out another series of experiments in which anesthesia is obtained not by local use but by injection behind the globe.

QUESTION FROM AUDIENCE: Has Dr. Smelser studied the effect of metycaine on the cornea and the effect of various anesthetics when combined with other drugs used in treatment of the cornea; for example, 5 per cent sulfathiazole is frequently used in conjunction with the anesthetic.

DR. BEAUMONT, New Zealand: I should like to ask Dr. Smelser what the effect of sodium bicarbonate would be.

DR. G. K. SMELSER: I do not know that I can answer Dr. Perera's question. I studied only the direct effect of these anesthetics on the cells; whether they act directly on the metabolism of these cells through their action on the nerve I do not know. That would be an interesting investigation. One can produce anesthesia by methods other than the application of these local anesthetics, and, so far as I am aware, they act in the same manner; that is, they retard cell division. However, the anesthesia itself does not necessarily inhibit the migration of epithelium. My co-workers and I have injected anesthetics subconjunctivally and have produced anesthesia by intraperitoneal injection, and the latter type of treatment does not inhibit cell migration or cell division, so far as we have studied it. The time required to complete a mitotic division may be affected. I have not done any experiments on the effect of the retrobulbar injection of drugs. Subconjunctival injection of cocaine or procaine or procaine combined with epinephrine was harmful to mitosis.

I have not done any experiments on the effect of bicarbonates.

I have not had any experience with metycaine. We have carried out experiments with the sulfonamide compounds, in exactly the same manner. We have studied their influence on both corneal burns and abrasions. Sulfathiazole by itself definitely inhibits mitosis and the migration of epithelium. We have also carried out experiments with sulfadiazine, which did not decrease cell division and when employed in ointment form or as fine crystals is not harmful. The corneal cells divide readily in the presence of sulfacetimide, but this drug inhibits cell migration. Penicillin is not at all harmful. The results of these experiments have been published in the *American Journal of Ophthalmology* (**27**: 1063 [Oct.] 1944).

Thrombosis of the Central Vein Treated with Heparin. DR. R. TOWNLEY PATON.

Heparin may be considered a rather harmless anticoagulant when properly administered.

The prognosis in cases of complete thrombosis of the central vein treated with heprain may still be considered as practically hopeless. In 4 out of 5 cases in which adequate treatment with the drug was carried out was finally necessary. In 10 cases of partial thrombosis of the central retinal vein treatment with heparin gave encouraging, but not dramatic, results.

No patient with recent thrombosis of the retinal vein should be denied the administration of heparin, unless study of a much larger series of cases proves it to be of doubtful value.

Regular Meeting, Dec. 18, 1944

A New Hemispheric Perimeter. DR. ARTHUR MINSKY.

A new instrument is presented and described which will enable the ophthalmologist to plot diplopia fields accurately, to test tropias, to determine peripheral fields, to plot detachments, to locate retinal tears and to prove the presence or absence of central color scotoma. A calibrated right angle dioptric scale enables him to evaluate the displacement of the plotted points without the use of prisms.

The instrument is a transparent, plastic hemisphere with a radius of 310 mm., stamped by degrees in the eight principal meridians. These markings are inconspicuous to the patient. Notations can be made on the hemisphere with temporary markings and the findings transferred to permanent records.

This perimeter has the following advantages: Measurements for tropias and diplopias are made at a constant fixed radius and in a constant meridian; the patient is oriented in space; the patient is under constant observation; the examination can be made rapidly; the instrument is portable and readily used in bedside examination; it has no moving parts or adjustable arm, and it is relatively inexpensive.

DISCUSSION

DR. THOMAS H. JOHNSON: This is an ingenious perimeter, and, so far as I know, this plastic arrangement is entirely new.

DR. WENDELL L. HUGHES, Hempstead, N. Y.: I should like to speak first about the background, which Dr. Minsky has not said much about.

On account of the uncontrolled background, visibility of a test object might vary in different portions of the field. One might be testing with a white object against a dull gray wall, where it might show up well in contrast; and if the object were moved farther up, it would show up very

poorly by contrast against a white ceiling. If the object were placed on a meridian so that it came in front of the examiner's dark coat during part of its excursion and against a light background in another part, variable results would be obtained. I wonder whether Dr. Minsky has made any provision for the lighting on the face of the test object. Is the illumination on the face of the object controlled? I think the idea is an ingenious one and will bear greater development.

DR. THOMAS H. JOHNSON: Dr. Wheeler, how do you think this instrument will compare with the tangent screen for the plotting of diplopia?

DR. MAYNARD C. WHEELER: It should be a convenient way to plot diplopia. I am sorry that Dr. Minsky has become tired of holding up prisms, for I do not think that his perimeter will replace them.

DR. ARTHUR MINSKY: We have not done any work on the background. I have used a light green wall, and it has worked rather effectively. Dr. Hughes's point about lighting is a good one, and I shall try to do something about it.

DR. THOMAS H. JOHNSON: Who will manufacture this perimeter?

DR. ARTHUR MINSKY: I do not know. I have been working on a plastic hemisphere for two years and could not obtain one which had the same thickness throughout until one of my friends got it for me. The perimeter will probably not be available for civilian use until the end of the war.

Test for Lability of Ocular Tension. DR. ROBERT K. LAMBERT and DR. SYLVAN BLOOMFIELD.

This paper will appear in full in a future issue of the ARCHIVES.

Iridencleisis for Glaucoma. DR. ALGERNON B. REESE.

This paper will appear in a future issue of the ARCHIVES.

Method for Extraction of Subluxated Lenses. DR. G. BONACCOLTO.

The method was presented accompanied with six colored slides portraying the main steps of the operation. Three moving pictures in color, representing 3 cases of dislocated lens, were shown.

The operation is preceded by lid sutures, substituted for the speculum, retrobulbar injection and suture of the superior rectus muscle. A conjunctival incision is made 2 mm. above the limbus and carried concentrically with it. Three double-armed silk sutures are passed 2 mm. from the limbus at 10, 12 and 2 o'clock. A keratome incision, at the superior limbus, is completed with scissors. The arms of the superior sutures are placed through the conjunctiva attached to the cornea. The conjunctival flap is firmly held with fine forceps, while the cataract loop is introduced into the vitreous and passed quickly behind the lens, pushing it against the cornea. This is done with a quick traction movement. The lens is expelled from the anterior chamber. The superior suture is gently tied, after which the auxiliary sutures are passed and tied. Seven patients were operated on with successful results.

DISCUSSION

DR. DAVID H. WEBSTER: This procedure is a distinct contribution to ophthalmology. I have seen Dr. Bonaccolto's results, and they are satisfactory. As long as the lens is visible while the patient is in a supine position, this technic is ideal, but the cases which present serious difficulties are those in which the lens floats freely in the vitreous and appears in the lower section of the vitreous when the patient is in an erect position, appears in the pupillary area or in the anterior chamber when the patient is in a prone position and drops back into the vitrous the moment the patient is turned in a supine position. I do not know whether it has been Dr. Bonaccolto's unfortunate experience to have to encounter such a case. Verhoeff, when this happened after he made his section, and the lens disappeared into the vitreous, directed his assistant to pour a stream of saline solution into the anterior chamber until the lens appeared where he could loupe it out. On several occasions Dr. David Webster Sr. turned the patient in a prone position, transfixed the lens by passing a knife needle, which entered the globe 8 mm. behind the limbus, and then turned the patient over in a supine position and completed the operation. I myself have operated in 2 such cases, in each instance assisted by the late Dr. H. R. Skeel. We placed the patient in a prone position, and we sat on the floor, made our incision and removed the lens, with slight loss of vitreous; in each instance the patient had 20/30 vision. Perhaps I am too old to try that now, but I believe it would be my operation of choice. I should like to know what Dr. Bonaccolto would do in a case in which he has a lens floating free in the vitreous.

DR. WENDELL L. HUGHES, Hempstead, N. Y.: In answer to Dr. Webster's question, the Hague lamp will render the lens brilliantly visible, so that it is illuminated the moment its edge is pushed into the pupil with the lens loop in the vitreous; then one can easily get the loop behind it because its location is so readily made out with good ultraviolet light.

DR. G. BONACCOLTO: I was going to suggest exactly what Dr. Hughes mentioned. With this light one can see the lens, and once it has been located it can be rather simply and safely extracted from the vitreous with the method I have just described.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. K. S. Sun.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, China.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Mr. John Foster, 45 Park Sq., Leeds.
Secretary: Mr. William M. Muirhead, 70 Upper Hanover St., Sheffield.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

Ophthalmological Society of South Africa

President: Dr. A. W. Sichel, National Mutual Bldg., Church Square, Cape Town.
Secretary: Dr. J. K. de Kock, Groote Kerk Bldg., 32 Parliament St., Cape Town.

Ophthalmological Society of the United Kingdom

President: Mr. Charles B. Goulden, 89 Harley St., London.
Secretary: Mr. Frank W. Law, 30 Devonshire Pl., London, W. 1.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

Royal Society of Medicine, Section of Ophthalmology

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

São Paulo Society of Ophthalmology

President: Prof. Moacyr E. Alvaro, Consolação 1151, São Paulo, Brazil.
Secretary: Dr. Silvio de Almeida Toledo, Enfermaria Santo Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

Scottish Ophthalmological Club

President: Dr. S. Spence Meighan, 13 Woodside Pl., Glasgow, C. 3.
Secretary: Dr. Alexander Garrow, 15 Woodside Pl., Glasgow, C. 3.
Place: Edinburgh and Glasgow, in rotation.

Sociedad Argentina de Oftalmologia

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

Sociedad Oftalmologia del Litoral, Rosario (Argentina)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Arturo Etchemendigaray, Villa Constitución, Santa Fé.
Place: Rosario. Time: Last Saturday of every month, April to November. All correspondence should be addressed to the President.

Sociedade de Oftalmologia de Minas Gerais

President: Prof. Hilton Rocha, Rua Rio de Janeiro 2251, Bello Horizonte, Minas Geraes, Brazil.
Secretary: Dr. Ennio Coscarelli, Rua Aimorés 1697, Bello Horizonte, Minas Geraes, Brazil.

Sociedade de Oftalmologia e Otorrinolaringologia de Rio Grande do Sul

President: Dr. Luiz Assumpção Osorio, Edificio Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul.
Secretary: Dr. Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul.

Sociedade de Ophthalmologia e Oto-Rhino-Laryngologia da Bahia

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

Società Oftalmologica Italiana

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

Société Française d'Ophtalmologie

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

Society of Swedish Ophthalmologists

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

Tel Aviv Ophthalmological Society

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

American Medical Association, Scientific Assembly, Section on Ophthalmology

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
In compliance with the request of the Office of Defense Transportation and in the interest of the national war effort a meeting will not be held in 1945.

American Academy of Ophthalmology and Otolaryngology, Section on Ophthalmology

President: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
President-Elect: Dr. Alan C. Woods, Johns Hopkins Hospital, Baltimore 5.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100–1st Ave. Bldg., Rochester, Minn.

American Ophthalmological Society

President: Dr. S. Judd Beach, 704 Congress St., Portland, Maine.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.

Association for Research in Ophthalmology, Inc.

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York.
Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.
Assistant Secretary-Treasurer: Dr. Hunter Romaine, 35 E. 70th St., New York.

Canadian Medical Association, Section on Ophthalmology

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

Canadian Ophthalmological Society

President: Dr. R. Evatt Mathers, 34½ Morris St., Halifax, N. S.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.

National Society for the Prevention of Blindness

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

Academy of Medicine of Northern New Jersey, Section on Eye, Ear, Nose and Throat

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark.
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

Central Illinois Society of Ophthalmology and Otolaryngology

President: Dr. Watson Gailey, 1000 N. Main St., Bloomington, Ill.
Secretary-Treasurer: Dr. William F. Hubble, 861-867 Citizens Bldg., Decatur, Ill.

Central Wisconsin Society of Ophthalmology and Otolaryngology

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

New England Ophthalmological Society

President: Dr. Paul A. Chandler, 5 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

Pacific Coast Oto-Ophthalmological Society

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

Puget Sound Academy of Ophthalmology and Oto-Laryngology

President: Dr. James H. Mathews, 1317 Marion St., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

Rock River Valley Eye, Ear, Nose and Throat Society

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

Saginaw Valley Academy of Ophthalmology and Otolaryngology

President: Dr. L. D. Gomon, 308 Eddy Bldg., Saginaw, Mich.
Secretary-Treasurer: Dr. Harold H. Heuser, 207 Davidson Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July, August and September.

Sioux Valley Eye and Ear Academy

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

Southern Medical Association, Section on Eye, Ear, Nose and Throat

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

Southwestern Academy of Eye, Ear, Nose and Throat

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

Southwestern Michigan Triological Society

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

Western Pennsylvania Eye, Ear, Nose and Throat Society

President: Dr. Ray Parker, 218 Franklin St., Johnston, Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

Arkansas State Medical Society, Eye, Ear, Nose and Throat Section

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

Colorado Ophthalmological Society

President: Dr. C. A. Ringle, 912–9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

Eye, Ear, Nose and Throat Club of Georgia

President: William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 526 Walton St., Macon.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

Kansas State Medical Society, Section on Ophthalmology and Otolaryngology

President: Dr. W. D. Pittman, Pratt.
Secretary: Dr. Louis R. Haas, 902 N. Broadway, Pittsburg.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Val. H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N. St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. George P. Meyer, 410 Haddon Ave., Camden.
Secretary: Dr. John P. Brennan, 429 Cooper St., Camden.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.
Secretary: Dr. Maxwell D. Ryan, 660 Madison Ave., New York 21.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. W. L. Diven, City National Bank Bldg., Bismarck.
Secretary-Treasurer: Dr. A. E. Spear, 20 W. Villard, Dickenson.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Pennsylvania Academy of Ophthalmology and Otolaryngology

President: Dr. Lewis T. Buckman, 83 S. Franklin St., Wilkes-Barre.
Secretary Pro Tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.
Time: Last week in April.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society, Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

Utah Ophthalmological Society

President: Dr. R. B. Maw, 699 E. South Temple, Salt Lake City.
Secretary-Treasurer: Dr. Charles Ruggeri Jr., 1120 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.

Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.

Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.

Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.

Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.

Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.

Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.

Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President: Each member, in alphabetical order.

Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.

Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. Michael J. Buonaguro, 589 Lorimer St., Brooklyn.

Secretary-Treasurer: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn 16.

Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. Walter F. King, 519 Delaware Ave., Buffalo.

Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.

Time: Second Thursday of each month.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.

Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.

Place: Mountain City Club. Time: Second Thursday of each month from September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Samuel J. Meyer, 58 E. Washington St., Chicago 2.

Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago 2.

Place: Continental Hotel, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.

Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.

Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman: Dr. Shandor Monson, 1621 Euclid Ave., Cleveland.

Secretary: Dr. Carl Ellenberger, 14805 Detroit Ave., Cleveland.

Time: Second Tuesday in October, December, February and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.

Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.

Time: Third Thursday of every month from October to April, inclusive.

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman: Dr. Erwin W. Troutman, 21 E. State St., Columbus, Ohio.

Secretary-Treasurer: Dr. T. Rees Williams, 380 E. Town St., Columbus 15, Ohio.

Place: University Club. Time: 6:15 p. m., first Monday of each month, from October to May, inclusive.

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. C. B. Collins, 704 Medical Professional Bldg., Corpus Christi, Texas.

Secretary: Dr. L. W. O. Janssen, 710 Medical Professional Bldg., Corpus Christi, Texas.

Time: 6:30 p. m., third Tuesday of each month from October to May.

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas 1, Texas.

Secretary: Dr. Tom Barr, Medical Arts Bldg., Dallas 1, Texas.

Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.

Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.

Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.

Secretary: Dr. Cecil W. Lepard, 1025 David Whitney Bldg., Detroit 26.

Place: Club rooms of Wayne County Medical Society.

Time: First Wednesday of each month, November to April, inclusive.

Detroit Ophthalmological Society

President: Dr. Raymond S. Goux, 545 David Whitney Bldg., Detroit 26.

Secretary: Dr. Arthur Hale, 1609 Eaton Tower, Detroit 26.

Place: Club rooms of Wayne County Medical Society. Time: 6:30 p. m., third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Appointed at each meeting.

Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.

Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.

Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.

Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Lyle J. Logue, 1304 Walker Ave., Houston, Texas.

Secretary: Dr. John T. Stough, 803 Medical Arts Bldg., Houston, Texas.

Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Oto-laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.

Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.

Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.

Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.

Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Dennis Smith, 623 Security Bldg., Long Beach 2, Calif.

Secretary-Treasurer: Dr. Robert Null, 710 Security Bldg., Long Beach 2, Calif.

Place: Seaside Hospital. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.

Secretary-Treasurer. Dr. K. C. Brandenburg, 110 Pine Ave., Long Beach 2, Calif.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.

Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Leon H. Guerin, 324 E. Wisconsin Ave., Milwaukee 2.

Secretary-Treasurer: Dr. Frank G. Treskow, 411 E. Mason St., Milwaukee 2.

Place: University Club. Time: 6:30 p. m., fourth Tuesday of each month from October to May.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.
Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.
Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Oto-laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Thomas H. Johnson, 30 W. 59th St., New York.
Secretary: Dr. Wendell L. Hughes, 131 Fulton Ave., Hempstead, N. Y.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Milton Berliner, 57 W. 57th St., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.
Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. D. D. Stonecypher, Nebraska City, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. Isaac Tassman, 136 S. 16th St., Philadelphia.
Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Secretary: Dr. Robert J. Billings, 509 Liberty Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. Michael J. Penta, 312 N. 5th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from September to July.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Peter N. Pastore, Medical College of Virginia, Richmond, Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. C. C. Beisbarth, 3720 Washington Blvd., St. Louis.
Secretary: Dr. H. R. Hildreth, 508 N. Grand Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting, 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.
Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.
Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.
Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.
Secretary: Dr. Clarence A. Veasey Jr., 421 W. Riverside Ave., Spokane, Wash.
Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. L. C. Ravin, 316 Michigan St., Toledo 2, Ohio.
Secretary: Dr. W. W. Randolph, 1838 Parkwood Ave., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. Harold M. Downey, 1740 M St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Richard W. Wilkinson, 1408 L St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.

CORRECTION

In the article by Major John G. Bellows entitled "The Crystalline Lens in Diabetes Mellitus," in the December 1944 issue (ARCH. OPHTH. **32:** 498-507), the statement on page 502, line 12, first column, "and later by Ascher" is incorrect. The reference to Dr. Ascher was concerned with an article on intraocular pressure in diabetic patients, and in that work no opinion was expressed that the lens was poisoned by a high concentration of dextrose.